8

Docket No.: 1611-010

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re US Patent No. 5,368,274:
Theodore J. Falk, et al.

Application No.: 07/946,392

Filed: September 17, 1992

Title: *Low Power Electromagnetic Valve*

Mail Stop Hatch-Waxman PTE
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

TRANSMITTAL LETTER

Dear Sir:

Transmitted herewith is an Application for Interim Patent Term Extension Under 35 U.S.C. § 156(d) and 37 C.F.R. § 1.710, Et. Seq. for U.S. Patent No. 5,368,274 and supporting papers. Three copies of the Application are submitted as duplicate originals. Also submitted herewith is a declaration related to this application.

The Commissioner is hereby authorized to charge the prescribed fee pursuant to 37 C.F.R. § 1.20(j)(2) for the initial application for interim extension in the amount of $420.00 fee to or credit overpayment to Deposit Account No. 18-1579 of the Marbury Law Group, PLLC.

Respectfully submitted,

Date: August 30, 2012

By

The Marbury Law Group PLLC
Customer Number: 22208
Telephone: 703-391-2900
Facsimile: 703-391-2901

Robert M. Hansen
Attorney for Applicants
Registration No. 43,656

09/04/2012 SSANDARA 00000017 181579 5368274
01 FC:1458 420.00 DA

I hereby declare further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under § 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any extension of patent term issuing thereon.

Respectfully submitted,

Date: August 30, 2012

By 

The Marbury Law Group PLLC
Customer Number: 22208
Telephone: 703-391-2900
Facsimile: 703-391-2901

Robert M. Hansen
Attorney for Applicants
Registration No. 43,656

Docket No.: 1611-010

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re US Patent No. 5,368,274:
Theodore J. Falk, et al.

Application No.: 07/946,392

Filed: September 17, 1992

Title: *Low Power Electromagnetic Valve*

Mail Stop Hatch-Waxman PTE
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION

I, Robert M. Hansen, a partner at The Marbury Law Group, PLLC and an authorized patent attorney for Applicant, Flowonix Medical, Inc., submit this declaration, along with an Application for Interim Patent Term Extension under 35 U.S.C. § 156(d) and 37 C.F.R. § 1.710, et seq. for U.S. Patent No. 5,368,274, and hereby state that:

1. I am a patent attorney authorized to practice before the Patent and Trademark Office and have general authority from the owner to act on behalf of the owner in patent matters as demonstrated by the attached Power of Attorney and recordation of change of corporate name;
2. I have reviewed and understand the contents of the application being submitted pursuant to 37 C.F.R. § 1.790;
3. I believe the patent is subject to extension pursuant to 37 C.F.R. § 1.790;
4. I believe an interim extension of the length claimed is fully justified under 35 U.S.C. § 156 and the applicable regulations; and
5. I believe U.S. Patent No. 5,368,274 meets the conditions for an interim extension of the term of a patent as set forth in 37 C.F.R. § 1.790.

PTO/SB/80 (11-08)
Approved for use through 11/30/2011. OMB 0651-0035
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

POWER OF ATTORNEY TO PROSECUTE APPLICATIONS BEFORE THE USPTO

I hereby revoke all previous powers of attorney given in the application identified in the attached statement under 37 CFR 3.73(b).

I hereby appoint:

☑ Practitioners associated with the Customer Number: 22208

OR

☐ Practitioner(s) named below (if more than ten patent practitioners are to be named, then a customer number must be used):

Name	Registration Number	Name	Registration Number

as attorney(s) or agent(s) to represent the undersigned before the United States Patent and Trademark Office (USPTO) in connection with any and all patent applications assigned only to the undersigned according to the USPTO assignment records or assignment documents attached to this form in accordance with 37 CFR 3.73(b).

Please change the correspondence address for the application identified in the attached statement under 37 CFR 3.73(b) to:

☑ The address associated with Customer Number: 22208

OR

☐ Firm or Individual Name			
Address			
City		State	Zip
Country			
Telephone		Email	

Assignee Name and Address:

Medasys Incorporated
500 International Drive, Suite 200
Mt. Olive, NJ 07828

A copy of this form, together with a statement under 37 CFR 3.73(b) (Form PTO/SB/96 or equivalent) is required to be filed in each application in which this form is used. The statement under 37 CFR 3.73(b) may be completed by one of the practitioners appointed in this form if the appointed practitioner is authorized to act on behalf of the assignee, and must identify the application in which this Power of Attorney is to be filed.

SIGNATURE of Assignee of Record
The individual whose signature and title is supplied below is authorized to act on behalf of the assignee

Signature		Date	6/21/11
Name	Steve Adler	Telephone	973 426 9229
Title	CEO, Medasys Inc.		

Electronic Patent Assignment System

Confirmation Receipt

Your assignment has been received by the USPTO.
The coversheet of the assignment is displayed below:

PATENT ASSIGNMENT

Electronic Version v1.1
Stylesheet Version v1.1

SUBMISSION TYPE:	NEW ASSIGNMENT
NATURE OF CONVEYANCE:	CHANGE OF NAME

CONVEYING PARTY DATA

Name	Execution Date
MEDASYS INCORPORATED	02/24/2012

RECEIVING PARTY DATA

Name:	FLOWONIX MEDICAL INCORPORATED
Street Address:	500 International Drive
Internal Address:	Suite 200
City:	Mount Olive
State/Country:	NEW JERSEY
Postal Code:	07828

PROPERTY NUMBERS Total: 17

Property Type	Number
Application Number:	11906826
Application Number:	10180708
Application Number:	11008446
Application Number:	12556184

Application Number:	12074570
Application Number:	12288659
Application Number:	12220593
Application Number:	09481298
Application Number:	10169821
Application Number:	07946848
Application Number:	08523083
Application Number:	08821602
Application Number:	07946392
Application Number:	08475773
Application Number:	08868389
Application Number:	12555257
Application Number:	61094449

CORRESPONDENCE DATA

Fax Number: (703)391-2901
Phone: 7033912900
Email: ptonotices@marburylaw.com
Correspondence will be sent to the e-mail address first; if that is unsuccessful, it will be sent via US Mail.
Correspondent Name: THE MARBURY LAW GROUP PLLC
Address Line 1: 11800 Sunrise Valley Drive
Address Line 2: 15th Floor
Address Line 4: Reston, VIRGINIA 20191

ATTORNEY DOCKET NUMBER:	1611-PAT
NAME OF SUBMITTER:	Robert M. Hansen
Signature:	/Robert M. Hansen/
Date:	04/10/2012

Total Attachments: 1
source=1611_NAME_CHANGE#page1.tif

RECEIPT INFORMATION

EPAS ID: PAT1918443
Receipt Date: 04/10/2012
Fee Amount: $680

Return to home page
Start another assignment from the same template

Delaware

The First State

I, JEFFREY W. BULLOCK, SECRETARY OF STATE OF THE STATE OF DELAWARE, DO HEREBY CERTIFY THE ATTACHED IS A TRUE AND CORRECT COPY OF THE CERTIFICATE OF AMENDMENT OF "MEDASYS INCORPORATED", CHANGING ITS NAME FROM "MEDASYS INCORPORATED" TO "FLOWONIX MEDICAL INCORPORATED", FILED IN THIS OFFICE ON THE TWENTY-FOURTH DAY OF FEBRUARY, A.D. 2012, AT 12:34 O'CLOCK P.M.

A FILED COPY OF THIS CERTIFICATE HAS BEEN FORWARDED TO THE NEW CASTLE COUNTY RECORDER OF DEEDS.

Jeffrey W. Bullock, Secretary of State

3912902 8100

120221191

AUTHENTICATION: 9388975

DATE: 02-24-12

You may verify this certificate online at corp.delaware.gov/authver.shtml

Docket No.: 1611-010

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re US Patent No. 5,368,274:
Theodore J. Falk, et al.

Application No.: 07/946,392

Filed: September 17, 1992

Title: *Low Power Electromagnetic Valve*

Mail Stop Hatch-Waxman PTE
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

INITIAL APPLICATION FOR INTERIM PATENT TERM EXTENSION UNDER 35 U.S.C. § 156(d)(5)

Please find contained herein Flowonix Medical, Inc.'s application (the application and accompanying documents are collectively referred to herein as the "Application") for interim extension of United States Patent No. 5,368,274 (referred to herein as the "Valve Patent") under 35 U.S.C. § 156(d)(5) and 37 C.F.R. § 1.790. The Valve Patent is owned by Flowonix Medical, Inc. ("Applicant"), which is located at 500 International Drive, Suite 200, Mount Olive, New Jersey 07828. The following information is provided pursuant to 37 C.F.R. § 1.710, et seq.

Applicant requests that a first interim extension of patent term of one year be granted and submits that the instant application is complete. For convenience and ease of reference, this Application is structured to correspond to the sections of 37 C.F.R. § 1.740, such that the paragraph numbers preceding each item correspond to the appropriate section of 37 C.F.R. § 1.740(a). Further, in accordance with the mandate of 37 C.F.R. § 1.790(b), Sections 1.740(a)(1), (a)(2), (a)(4), and (a)(6)–(a)(17) and 37 C.F.R. § 1.741 are read in the context of the product currently undergoing review. Section 1.740(a)(3) and (5) are not applicable to the request for interim extension.

(1) **Exhibit A** provides a complete identification of the medical device currently undergoing review (hereinafter, the "Medical Device"), including its physical structure or characteristics. The Medical Device is intended to be commercially marketed under the trade name of Prometra® Programmable Pump System, and is an implantable drug delivery pump intended to be implanted in patients who require long-term, frequent administration of a drug. The Medical Device has been under review by the Food and Drug Administration (FDA) since 2006. As the materials in **Exhibit A** will show, the Medical Device's essential component is its valve-accumulator subsystem, which comprises a pair of valves as claimed in U.S. Patent No. 5,368, 274 (the "Valve Patent"). These valves work in concert to regulate with precision the amount of drug that is administered to the patient, regardless of external changes in pressure and temperature. As **Exhibit A** discusses, the means by which an implantable pump regulates dosing "is the most mechanically complex component of an implantable pump and has significant impact on several pump features." The low energy consumption of the valves and lack of considerable moving parts of the valves claimed in the Valve Patent extend the life of the Medical Device, which is a key consideration in an implantable device. Thus, the valves claimed in the Valve Patent are crucial to the overall functionality of the Medical Device.

(2) The Medical Device (i.e., the Prometra® Implantable Pump System) is a class III device that requires a Premarket Approval Application under section 515 of the Federal Food, Drug and Cosmetic Act. Therefore, Applicant is and has been pursuing approval of the Medical Device under § 515 of the Federal Food, Drug, and Cosmetic Act.

(3) Not applicable to interim extension applications. While the FDA did send a letter approving Applicant's PMA on February 7, 2012, the FDA has not, to date, given Applicant final permission to use or market the Medical Device commercially. See **Exhibit F** for a more thorough explanation. The letter dated February 7, 2012 from the FDA is attached as **Exhibit I.**

(4) Not applicable to requests for extension for medical devices.

(5) Not applicable to interim extension applications. However, this interim extension application is being filed within the window of six months prior to the expiration of the term of the patent and fifteen days prior to the expiration of the term of the patent as prescribed in 35 U.S.C. § 156(d)(5)(A). The patent term is to expire on September 17,

2012, with the last day on which the Application for filing the interim extension request falling on September 2, 2012.

(6) This Application is for United States Patent No. 5,368,274. The subject matter of the Valve Patent was invented by Theodore J. Falk, W. Richard Brown, Lawrence E. Morris, and Norbert W. Frenz, Jr. The Valve Patent was assigned to Flowonix Medical, Inc. by Medasys Incorporated on February 24, 2012, and that assignment was recorded on April 10, 2012. A list of all assignments of the Valve Patent is attached as **Exhibit B**. The Valve Patent issued on November 29, 1994 and is due to expire on September 17, 2012.

(7) A copy of the Valve Patent, including the specification (including claims) and drawings is attached as **Exhibit C.**

(8) Maintenance fees were paid on the Valve Patent on March 9, 1998; May, 21, 2002; and May 24, 2006 to maintain the term of the patent until September 17, 2012. A copy of the receipt for the maintenance fees for the Valve Patent is attached as **Exhibit D.** A Certificate of Correction was issued on April 18, 1995. A copy of the certificate of correction is also included in **Exhibit D**. No disclaimer or reexamination certificate applies to the Valve Patent.

(9) The Valve Patent contains 28 claims. As required by 37 C.F.R. § 1.740(a)(9)(i), Applicant submits that at least claims 1–10, 12–13, 15–21, 24–25, and 27–28 of the Valve Patent read on the valves utilized in the Medical Device. Pursuant to 37 C.F.R. § 1.740(a)(9)(i) and MPEP § 2753, a demonstration of the manner in which at least independent claim 1 reads on the Medical Device is attached as **Exhibit E.**

(10) Pursuant to 37 C.F.R. § 1.740(a)(10)(v), a statement beginning on a new page of the relevant dates and information pursuant to 35 U.S.C. § 156(g) is attached as **Exhibit F.**

(11) Flowonix Medical, Inc. was formerly known as Medasys Inc., which was formerly known as InSet Technologies Incorporated. A brief description of the significant activities undertaken by Applicant and its predecessors in interest, InSet Technologies Incorporated and Medasys, Inc., to market products covered by the Valve Patent is attached as **Exhibit G.**

(12) A statement that, in the opinion of the Applicant, the patent is eligible for the extension and a statement regarding the length of extension claimed, including how the length of extension was determined is attached as **Exhibit H.**

(13) Applicant acknowledges its duty to disclose to the Commissioner of Patent and Trademarks and the Secretary of Health and Human Services or the Secretary of Agriculture any information that is material to the determination of entitlement to the extension sought, and the tenets of the duty of disclosure in 37 C.F.R. § 1.765 relevant to the application.

(14) The Commissioner is authorized to charge the fee in 37 C.F.R. § 1.20(j)(2) or any additional fee, or credit overpayment, to Deposit Account No. 18-1579.

(15) Any inquires and correspondence relating to this application should be directed to the following:

Robert M. Hansen, Esq.
The Marbury Law Group, PLLC
11800 Sunrise Valley Drive, 15th Floor
Reston, VA 20191-5302
703-391-2900 Firm Telephone
571-267-7003 Direct Line
703-391-2901 Facsimile
703-909-5155 Cell
RHansen@MarburyLaw.com

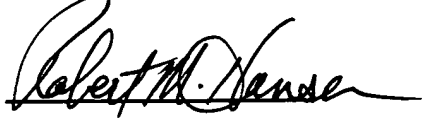
Applicant is asking for an interim extension of U.S. Patent No. 5,368,274 until the earlier of sixty days following Regulatory Approval of the Medical Device or September 17, 2013.

If there are any questions regarding this application, please contact the agent for Applicant, as noted above.

Signatory below is authorized to sign this Application on behalf of Applicant pursuant to a Power of Attorney signed by an authorized agent of Applicant.

Respectfully submitted,

Date: August 30, 2012

By 

The Marbury Law Group PLLC
Customer Number: 22208
Telephone: 703-391-2900
Facsimile: 703-391-2901

Robert M. Hansen
Attorney for Applicants
Registration No. 43,656

EXHIBIT A

Product Description

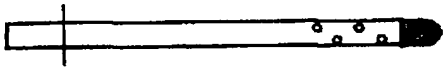
CONTENTS

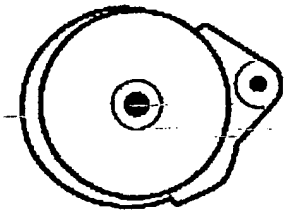
MEDASYS™

Implanting Confidence

PATIENT GUIDE

For use with Prometra® Programmable Pump System





Caution: Federal Law (USA) restricts this device to sale by or on the order of a physician.

Table of Contents

Glossary

Abdomen: soft space between your ribs and hip bones
Arachnoid: the middle protective membrane covering the brain and spinal cord
Anesthesia: medicine that causes you to lose your ability to sense pain, among other sensations
Bolus: large or concentrated dose of medicine
Cardioversion: electrical "jump start" for your heart to correct irregular rhythms. Also may be done with medication(s).
Catheter: tiny flexible tube
CSF: cerebrospinal fluid
Chronic: long-term
Contrast media: dye that can be seen under x-ray
CT: non-invasive, non-magnetic scan used to verify intrathecal catheter position
DEHP: Bis(2-ethylhexyl)phthalate, a plasticizer in PVC
Defibrillation: stopping the heart from quivering, "fibrillating", instead of pumping normally. Often done by applying electricity via small paddles but may also be done with medication(s).
Dura Mater (Dura): the outermost protective membrane covering the brain and spinal cord
Epidural: located outside the dura mater or anesthesia injected into this space.
Explant: to take out; opposite of implant
FDA: US Food and Drug Administration
Fiddling: rotating the pump in the pocket created for it in the abdominal wall
Hyperbaric: the medical use of oxygen at a level higher than atmospheric pressure.
Implant: to put in
Inflammatory mass: group of inflamed cells
Intractable: difficult-to-manage; hard to treat, relieve, or cure
Intrathecal space: fluid-filled area around the spinal cord
Latex: natural rubber
Orally: by mouth
Palpable: that which can be felt by touching
PVC: polyvinyl chloride, a plastic material
Programmable: ability to be controlled remotely
Prometra: brand name for Medasys' programmable drug delivery pump and pump system
Saline: Salt water balanced to match your body's composition
Telemetry: remote transmission of data
Vertebra/Vertebral Body: bones or segments which make up the spinal column and through which the spinal cord runs

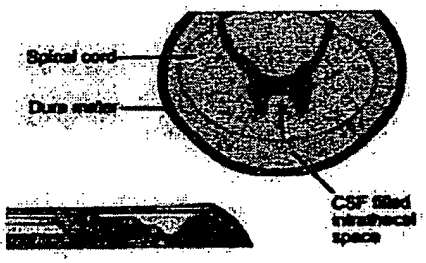
Descriptive Information

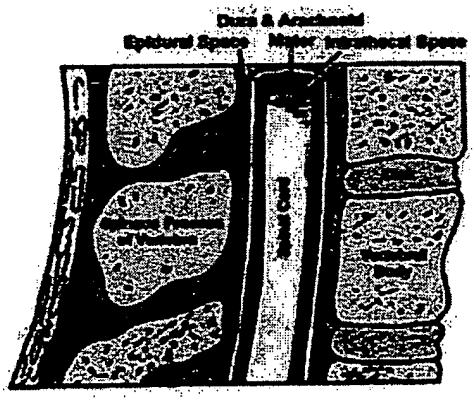
Your doctor is recommending this treatment for you because your prior treatments have not been adequate. This Patient Guide will help you understand your Prometra Programmable Pump System and help answer your questions about this treatment. However, it is only a guide and **your doctor and nurse are always your best source of information.** Be sure to ask them to explain anything that is unclear. And, always follow their directions concerning your Prometra Programmable Pump System.

Note: The use of the terms "medication" and "drug" throughout this document refer to the use of Infumorph® which is the Food and Drug Administration (FDA) approved brand name for Morphine Sulfate.

Potential Benefits of the Prometra Programmable Pump System

Your spinal cord is the main pathway for information connecting your brain and all the rest of the nerves in your body. If you take a pill orally (by mouth), medicine has a much harder time reaching the spinal cord as much of the drug is absorbed by your body along the way. Delivering this dose directly to your spinal cord reduces the amount of medication needed. For example, published studies show that you can take 1/100th of your pain medication when it is delivered to your **intrathecal space (fluid-filled space around your spinal cord)** and achieve the same result.[1] With a much smaller intrathecal dosage, your side effects may be reduced. Or, your doctor may be able to increase your dosage without as many side effects.





[1] Rauck R, Intrathecal drug delivery. Seminars in Pain Medicine, 2004; 2(1): 2-7.

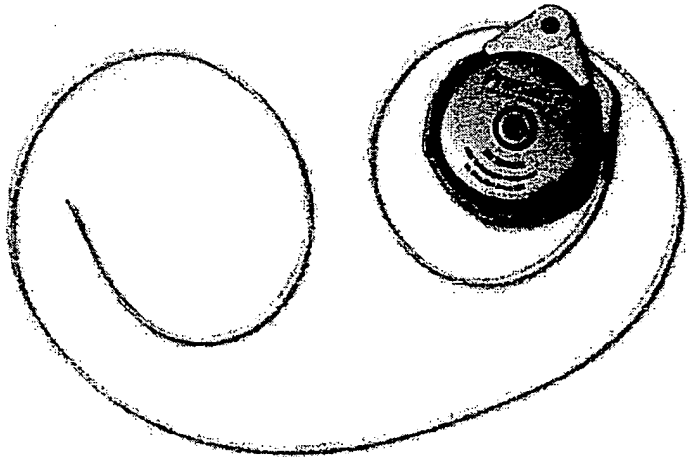
Purpose of the device (FDA approved indications for use)

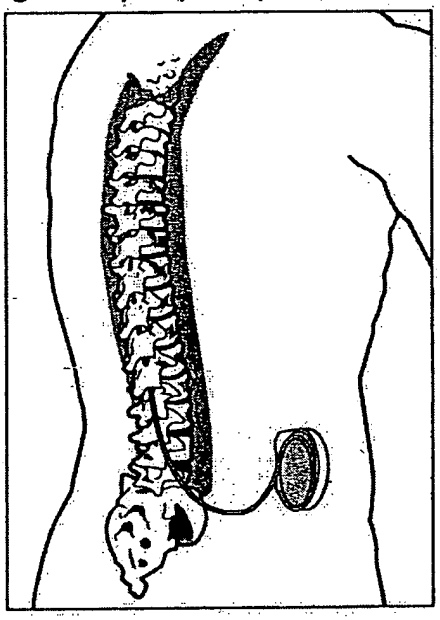
Your Prometra Programmable Pump System is approved to infuse Infumorph® (preservative-free morphine sulfate sterile solution) directly into the intrathecal space. Sterile preservative-free saline (salt water) solution may also be used in your pump.

Please read the drug label for information on Infumorph. The National Library of Medicine at www.nlm.nih.gov is a good source for this information.

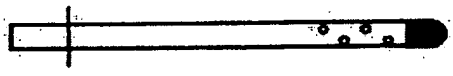
Description of the device

The Prometra Programmable Pump System infuses the drug directly to your spinal cord.

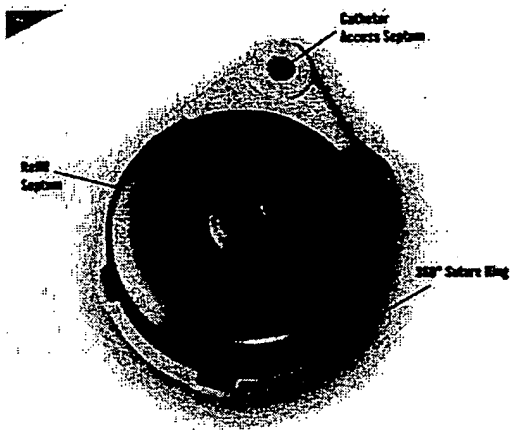




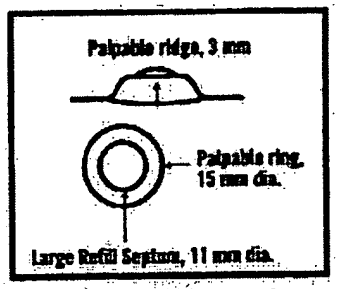
A thin intrathecal catheter with holes near the end is carefully placed in your intrathecal space and securely connected to the Prometra programmable pump implanted in your abdomen (the soft space between your ribs and hip bones). Your catheter has a radiopaque tip that can be seen under x-ray.



The pump has a central refill septum that a nurse or doctor can feel underneath your skin (palpate). Your medicine will be refilled every 30-90 days by accessing this refill port with a thin needle. If needed, the nurse or doctor may access your catheter directly to provide a bolus (large or concentrated dose) of medicine through the catheter access septum.



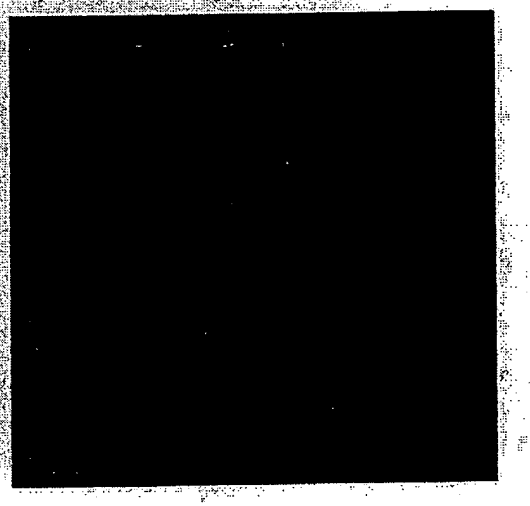
Easy Refill Septum



And, rated to 1,000 + punctures.

When you initially receive the pump, and at most refills, the nurse or doctor will use a handheld programmer, like a remote control, to set how much medicine to deliver and at what times. Your programmable pump can deliver different amounts of medication at different times of the day, such as more at night while you are sleeping and less during the day.

Prometra Programmer



Making the Decision if the Pump is Right for You

Contraindications

The pump system should not be implanted:

- If you have an infection, such as a tooth abscess or a bed sore.
- If your body type cannot comfortably or safely accommodate the pump size and weight.
- If the pump cannot be implanted under your skin 2.5 cm (1 in.) deep.
- If you have allergies to the catheter materials, including silicone elastomers, barium sulfate, tungsten, polyacetal resin, ink, stainless steel, hydroglide hydro gel coating, or plastic needle hubs (polypropylene and acrylic based).

- If you have allergies to the pump materials, including titanium, silicone elastomers, polyphenylsulfone, silicone adhesive, polyvinylidene fluoride, MP35N metal (nickel-cobalt-chromium-molybdenum alloy), or stainless steel (AL29-4, 316L).
- If you have exhibited a prior intolerance to implanted devices.
- If your spinal column anatomy obstructs cerebrospinal fluid flow or prevents intrathecal drug delivery.
- If you are deemed an unsuitable candidate after psychological evaluation.
- If you have any contraindication to Infumorph as per the approved drug labeling. The National Library of Medicine at www.nlm.nih.gov is a good source for FDA-approved drug information.

Warnings

WARNING: USE OF UNAPPROVED DRUGS (e.g., DRUG COCKTAILS, PHARMACY-COMPOUNDED DRUGS, MORPHINE WITH PRESERVATIVES, ETC.) WITH THE PROMETRA PUMP COULD RESULT IN PUMP FAILURE AND/OR SERIOUS ADVERSE EVENTS INCLUDING DEATH.

WARNING: YOU SHOULD NOT UNDERGO MRI OR OTHER MAGNETIC THERAPIES. FAILURE TO EMPTY THE PUMP PRIOR TO EXPOSURE TO MRI ENVIRONMENT COULD RESULT IN DRUG OVERDOSE THAT COULD LEAD TO SERIOUS PATIENT INJURY OR DEATH.

- You should not undergo hyperbaric therapy since exposure could result in drug underdose.
- In the event of over-medication, refer to the approved Infumorph labeling for appropriate treatment.
- Clinicians implanting, programming, accessing, or maintaining implanted programmable pumps must comply with the instructions for use. Technical errors may result in a return of underlying symptoms, drug withdrawal symptoms, or clinically significant or fatal overdose.
- Do not incinerate or cremate the pump.
- You should not have an occupation where you would be exposed to high current industrial equipment, powerful magnets or transmitting towers, such as, electricians, electrical engineers or MRI technicians.
- Avoid powerful magnets, such as MRI or other magnetic therapies. Exposing your pump to powerful magnets may result in a fatal overdose. In an emergency requiring an MRI or exposure to powerful magnets, your doctor must completely empty your pump of all medication and allow you to have an MRI. The pump cannot be used after exposure to MRI. If an MRI procedure has been utilized the pump should be explanted.

Precautions

General:

- Carefully read all instructions prior to use. Follow all instructions.
- Certain equipment may cause electrical noise, which may interfere with programming. If suspected, move the patient from the suspected source of interference to facilitate the programming procedure. Examples of equipment that may cause inference include: radio, TV, cellular phones, telemetry, amateur radio, radio navigational aids, industrial scientific medical devices (ISM), large electric motors, etc.
- Do not use accessories that are not referenced in these instructions for use. Only use devices and accessories that are referenced for use with the Prometra® Programmable Pump in these instructions.
- Safety and effectiveness for use in pediatric patients under 22 years old has not been investigated or established.
- The effects of implanting this device in patients with other implanted medical devices, other than neurostimulators, are unknown.
- Pain on injection that was not noted during previous injections may be an early sign of infection.

Implant:

- Implantation of this device and subsequent use, reprogramming, and refill should only be conducted by qualified medical personnel specifically trained for surgical implantation, use, and maintenance of the device. Use of this device by non-qualified or untrained personnel could lead to serious consequences involving under- or over- dosage of Infumorph. In the event of over-medication, refer to the approved Infumorph labeling for appropriate treatment.
- If therapy is discontinued for an extended period, the pump should be emptied of Infumorph and filled with a preservative-free 0.9% sterile saline solution and programmed to a low infusion rate to maintain catheter patency.

Device Compatibility:

- **Pump accessories.** Only use the Prometra Programmable Pump with the accessories listed in these instructions for use. Use of alternate accessories may result in damage to Prometra components, less than adequate therapy, or increased risks to the patient.
- **Pump.** Only use with Prometra Programmer.
- **Therapeutic ultrasonics or lithotripsy** - Use of therapeutic ultrasonic devices, such as electrohydraulic lithotriptors, has not been tested on the Prometra pump. If lithotripsy must be used, do not focus the beam in proximity of the pump.

- **Medical devices.** The Prometra Pump Programmer may affect other medical devices. Use or interference with medical devices, other than neurostimulators, has not been established.
- **Applied electric currents.** Interaction of the Prometra Pump with electric currents applied to the body such as cardioversion or defibrillation has not been established. Care must be exercised if you receive these treatments. Where practical, the pump should be turned off before application of electric currents to your body. Confirmation that the pump programming has not changed must be carried out as soon as possible after the procedure.
- **Radiation.** Do not use radiation therapy in the area of the pump. The effects of ionizing radiation on the Prometra Pump have not been established, and these therapies may have effects on pump operation that are not immediately apparent.

Risks

Potential Adverse Events

The use of implanted pumps provides an important means of delivering Infumorph directly to your spine. However, the potential exists for serious complications including the following:

Possible Risks Associated with Programmable Implantable Pump

- Adverse reaction to pump materials
- Battery depletion
- Bleeding
- Body rejection phenomena
- Defective pump (e.g. propellant chamber leakage, pump rupture)
- Inability to locate septum
- Inability to program pump due to programmer failure or loss of telemetry
- Inflammation, necrosis, or scarring of skin over implant area
- Programming errors, resulting in over or under dosing
- Pump flipping or twisting
- Pump implanted too deep, resulting in difficulty accessing or inability to access port
- Pump migration (moving within your body)
- Pump pocket pain/soreness
- Pump pocket seroma/hematoma, with or without infection
- Pump rotation
- Pump site skin erosion (pump rubs through your skin)
- Pump stoppage
- Refill errors, including injection into pump pocket, injection into wrong port, incorrect volume, incorrect concentration, difficulty accessing pump port
- Septum dislodgement
- Septum leakage

- Slow, erratic or fast flow
- Software error

Possible Risks Associated with Intrathecal Catheter

- Catheter disconnection
- Catheter kinking
- Catheter fracture
- Catheter migration (moving within your body)
- Cerebrospinal fluid (CSF) leak
- Disconnection
- Erosion (catheter rubs through your skin)
- Fibrosis (scarring)
- Infection in intrathecal space, including meningitis
- Inflammatory mass formation (e.g., granuloma)
- Malpositioning
- Nerve damage
- Pain on injection
- Poor radiopacity
- Post dural puncture headache (post surgical headache)
- Reaction to catheter materials
- Reversible or irreversible partial or complete occlusions (blockages)
- Spinal cord pressure leading to paralysis
- Spinal cord trauma, perforation, laceration
- Subcutaneous catheter tract infection
- Subcutaneous tunnel infection
- Tears/breaks

In rare instances, the development of an inflammatory mass at the tip of the implanted catheter may occur, which can result in serious neurological impairment. Patients should be monitored carefully at each visit for any new neurological signs or symptoms, including:

- progressive change in the character, quality, or intensity of pain
- an increase in the level and degree of pain despite dose escalation
- sensory changes (i.e., numbness, tingling, burning)
- hyperesthesia and/or hyperalgesa

Presentations that require immediate diagnosis include

- Burning, numbness, or tingling
- Increase in pain despite dose escalation
- Increased sensitivity to stimuli or pain
- Progressive change in the type or amount of pain
- Bowel and/or bladder dysfunction
- Gait disturbances or difficulty ambulating

- Paraparesis or paralysis

If the presence of an inflammatory mass is suspected, recommended evaluation should include a review of the patient history and neurological evaluation, radiological diagnostic procedures (such as a CT scan with contrast) and appropriate clinical consultation.

Inflammatory mass has been associated with a wide range of doses and concentrations of opioids. No dose or concentration of Infumorph can be considered completely free of risk from inflammatory mass. The risk of inflammatory mass occurrence appears to be cumulative over time and increases with higher concentrations and doses of opioids.

Common Side Effects of Infumorph

- If nausea occurs, consult your doctor or pharmacist for ways to decrease it (such as taking antihistamines, lying down for 1 to 2 hours with as little head movement as possible).
- This medication may cause dependence, especially if it has been used regularly for a long time or in high doses. In such cases, withdrawal reactions (such as restlessness, watery eyes, widened pupils, sweating, and runny nose) may occur if you suddenly stop this drug. To prevent withdrawal reactions, your doctor may reduce your dose gradually. Consult your doctor or pharmacist for more details, and report any withdrawal reactions immediately.
- When this medication is used for a long time, it may not work as well. Your doctor may need to increase your dose or change your medication. Talk with your doctor if this medication stops working well.
- Along with its benefits, this medication may rarely cause abnormal drug-seeking behavior (addiction). This risk may be increased if you have abused alcohol or drugs in the past. Use this medication exactly as prescribed to lessen the risk of addiction.
- Tell your doctor if your pain persists or worsens.
- Nausea, vomiting, constipation, lightheadedness, dizziness, drowsiness, increased sweating, or dry mouth may occur. Pain, redness, or swelling at the injection site may occur if this medication is given into a muscle or under the skin. If any of these effects persist or worsen, tell your doctor or pharmacist promptly.
- To prevent constipation, maintain a diet adequate in fiber and drink plenty of water, if not contraindicated. If necessary, consult your doctor for help in selecting a laxative (such as a stimulant type with stool softener).
- Remember that your doctor has prescribed this medication because he or she has judged that the benefit to you is greater than the risk of side effects. Many people using this medication do not have serious side effects.
- Tell your doctor immediately if any of these unlikely but serious side effects occur: slow/shallow breathing, fainting, mental/mood changes (such as agitation, hallucinations, confusion), difficulty urinating, vision changes, slow/fast heartbeat.

- Tell your doctor immediately if any of these rare but very serious side effects occur: severe stomach/abdominal pain, change in the amount of urine, seizures.
- A very serious allergic reaction to this drug is rare. However, seek immediate medical attention if you notice any symptoms of a serious allergic reaction, including rash, itching/swelling (especially of the face/tongue/throat), severe dizziness, trouble breathing.
- This is not a complete list of possible side effects. If you notice other effects not listed above, contact your doctor.

Benefits

Implantation of the Prometra programmable pump system is often used when conventional treatment is no longer effective. Benefits you may expect include:

- Accurate delivery of the prescribed dosage
- Delivery of Infumorph which is intended for intraspinal administration in the management of pain.

Before, During and After Your Procedure

Your Pump Implant Surgery

The Prometra Programmable Pump System will be placed in your body during a surgical procedure that is usually about 1 hour long. You will be given anesthesia which will allow you to sleep through the surgical procedure without pain. Your doctor will give you specific instructions about how to prepare for the surgery.

Both the pump and catheter are implanted under your skin. A small incision is made in your back to provide access to your spinal canal. The tip of the catheter is threaded up your spine into your intrathecal space while using a form of x-ray. Your doctor usually places the pump at about waist level (abdomen), above your hip bone and below your ribs, and to one side. The catheter is tunneled underneath your skin from where it enters your spine around your waist to the pump. The catheter length is then customized to your body and connected to the pump. Your doctor may chose to use sutures near where the catheter enters your spine. This will help the catheter to maintain its position.

Your pump will be filled and programmed to deliver your medication at either a constant or variable rate, or it can be set to give a dosage repeated at specified times. Your doctor will determine the best medication schedule for you.

When you wake up, you will notice two incisions. Your doctor made one incision in your abdomen to place the pump. Another small incision is made in your back to position the catheter in your spine.

Follow-up Visits

Your first follow-up visit will be scheduled one to two weeks after surgery. At this visit, your doctor will look at the surgical site and review the medication therapy plan that was started when you received your pump.

Refills

Your doctor will schedule regular pump refill visits as needed so that your pump does not run out of medication. This is usually about every 30-90 days. Only your doctor or nurse can program your pump to deliver medication. **It is important not to miss a refill appointment.** You should always let your doctor know as soon as possible if you think you will miss an appointment. This will allow time for a new appointment to be set or for other arrangements to be made. If your pump is not refilled on time, it may become empty, and you will not get your required medicine. When you run out of medicine, your symptoms can range from fairly minor to very serious depending on the medicine you were receiving. Refer to the Infumorph prescribing information for the withdrawal or underdose symptoms to expect if your pump runs out of medication or if you stop getting medicine from the pump for any reason.

To refill your pump, your doctor will insert a special needle of just the right size and length into your pump through the center refill septum. For most patients this causes only a mild pricking sensation. Then, your doctor or nurse will completely empty your pump. Your pump must be emptied to measure the amount of medication that was left in the pump. This allows verification that the pump has been delivering the right amount of medicine to your spinal cord. Your doctor will then refill your pump by attaching a syringe and tubing set filled with your medication to the special needle and pushing the medication into the pump reservoir. Then, your doctor or nurse will program the pump to deliver your medication using the programmer. Once the pump is refilled and programmed by your doctor, the pump will automatically deliver the medication at the programmed dosage rate.

What should I expect after surgery?

After surgery you may have some redness and tenderness in the area where your incision was made. This will normally go away in a few weeks. However, contact your doctor or nurse if you notice unusual changes in the skin area over the pump such as increased swelling, redness, or soreness.

For the first few days after you receive the pump, you should avoid heavy exertion and strenuous activities such as lifting or pushing, carrying anything heavy, running, and swimming. Follow all your doctor's instructions about your pump. Once your incision heals, you should be able to resume normal daily activities such as bathing and exercising.

Will I need to wear a bandage over the pump?

A bandage will be required until your incision heals. After a refill visit, a bandage may be used over the area where the needle was inserted.

Will others know that I have a pump?

After your incision heals, the pump will likely protrude slightly from your abdomen. In thinner people, it tends to protrude more and in larger people, it is less obvious. Your doctor may be able to provide pictures of what the pump looks like in different body types.

Do I have to wear certain types of clothing?

This depends on where your pump is placed. You should avoid clothing that would rub or be tight over the incision site immediately after surgery. Wear loose, comfortable clothing the day of your implant surgery. After the incisions heal, you should be able to wear your normal clothing.

Can I move my pump, e.g. if it is uncomfortable?

Your pump has been placed with the refill septum facing up so it can communicate with the programmer in your doctor's office. Never move, twist or turn your pump (fiddling). This may flip your pump or cause damage to the catheter. Either of these may interfere with delivery of your medication or require reoperation. However, typical movement should not result in damage to the catheter or pump.

How do I know if my pump still works after I bump it or if I fall? What about my catheter?

A slight bump is unlikely to affect your pump or catheter. However, if you hurt yourself when you fell, you may have hurt the pump or catheter. If you experience much more pain or notice unusual symptoms, contact your doctor immediately. To verify if your pump and catheter are working, your doctor or nurse will check the amount of medication left in the pump. If too much is left, they may perform an x-ray or CT to verify proper catheter and pump position.

Will my pump set off metal detectors? Is security "wanding" safe?

It may. And, as some personnel are not familiar with the implant card with which you will be provided, you may be asked to show them the pump site. Please consider this when dressing for court appointments, air flights and other facilities where metal detectors might be encountered. If you need to be "wanded" by security personnel, e.g. at the airport, the pump programming will not be affected.

What should I do if I hear my pump beeping or making noise?

Your Prometra programmable pump has two alarms. Both alarms use the same beeping tone but have a different beep length and different number of beeps in a group. **Contact your doctor immediately if you hear these alarms.**

The **Low Reservoir Alarm** warns you when the medication in the pump reservoir gets below a certain volume. Your doctor can set this volume, and the alarm can be turned on using the programmer. If the alarm is on and the reservoir volume gets low, the pump sounds two

short beeps every 30 minutes. The alarm continues to sound until your doctor turns it off using the programmer or refills your pump.

The **Critical Error Alarm** indicates that the pump has stopped delivering medication. The pump sounds three long beeps every 30 minutes. This alarm occurs any time the pump is not delivering medication, including a low pump battery. Once the **Critical Error Alarm** has occurred, the pump stops pumping medication. Your doctor cannot turn off the alarm with the programmer. Your pump will keep beeping until it is replaced or until the battery runs completely out of power. There is no way to replace the battery only. The pump must be disconnected from the catheter and replaced. A new pump can be implanted and connected to the original catheter. Contact your doctor as soon as possible to schedule pump replacement surgery or to assess therapy alternatives.

Will the use of cell phones, a microwave oven, or other household electrical devices interfere with my pump?

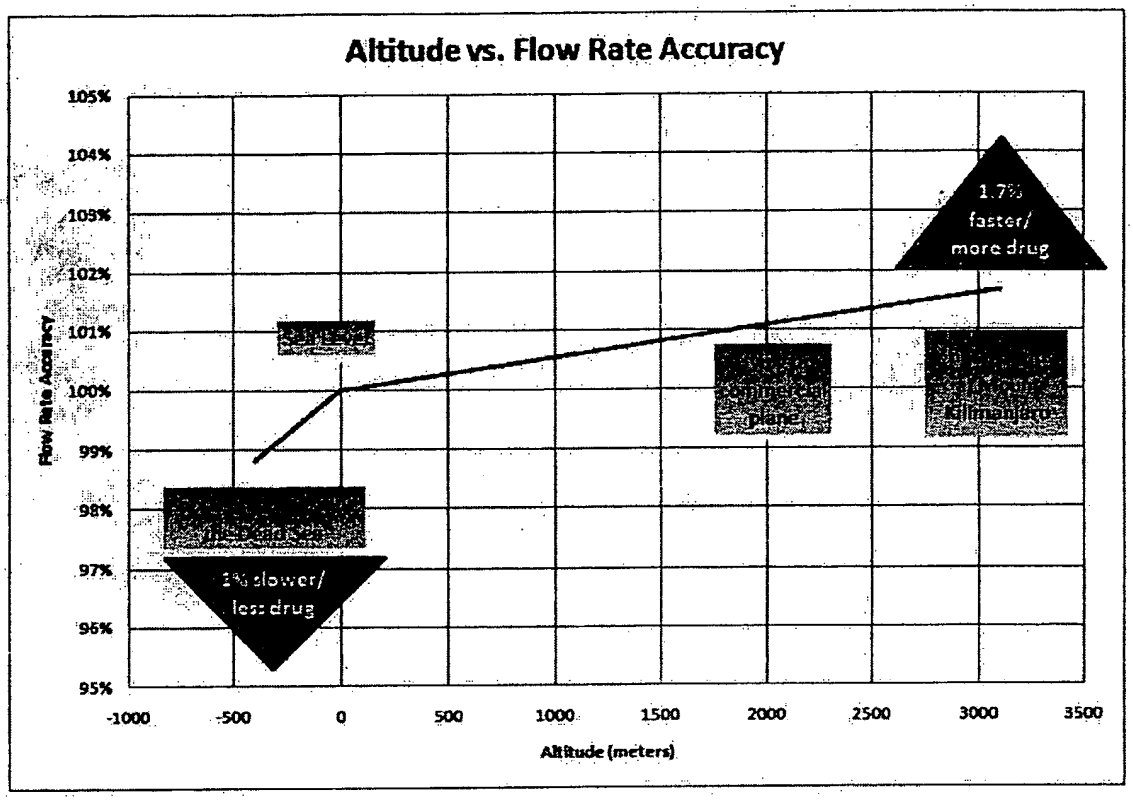
No. Your pump is designed so that cell phones, microwaves, or other household appliances and items that you may use in your normal daily life will not affect it. If you suspect interference with your pump, move away from or turn off the electrical device. Your pump will not be permanently affected.

Do pressure changes affect my pump?

The Prometra programmable pump has a special design which isolates the drug reservoir from most pressure changes, making it ***immune to most pressure changes***. You are free to enjoy, with your doctor's permission:

- Flying
- Mountain hikes up to 10,000 feet
- Skiing up to 10,000 feet
- Snorkeling within 15 feet of the surface
- Swimming within 15 feet of the surface

These activities are SAFE and WILL NOT AFFECT YOUR PUMP. Always consult your doctor first about any other activities not listed here.



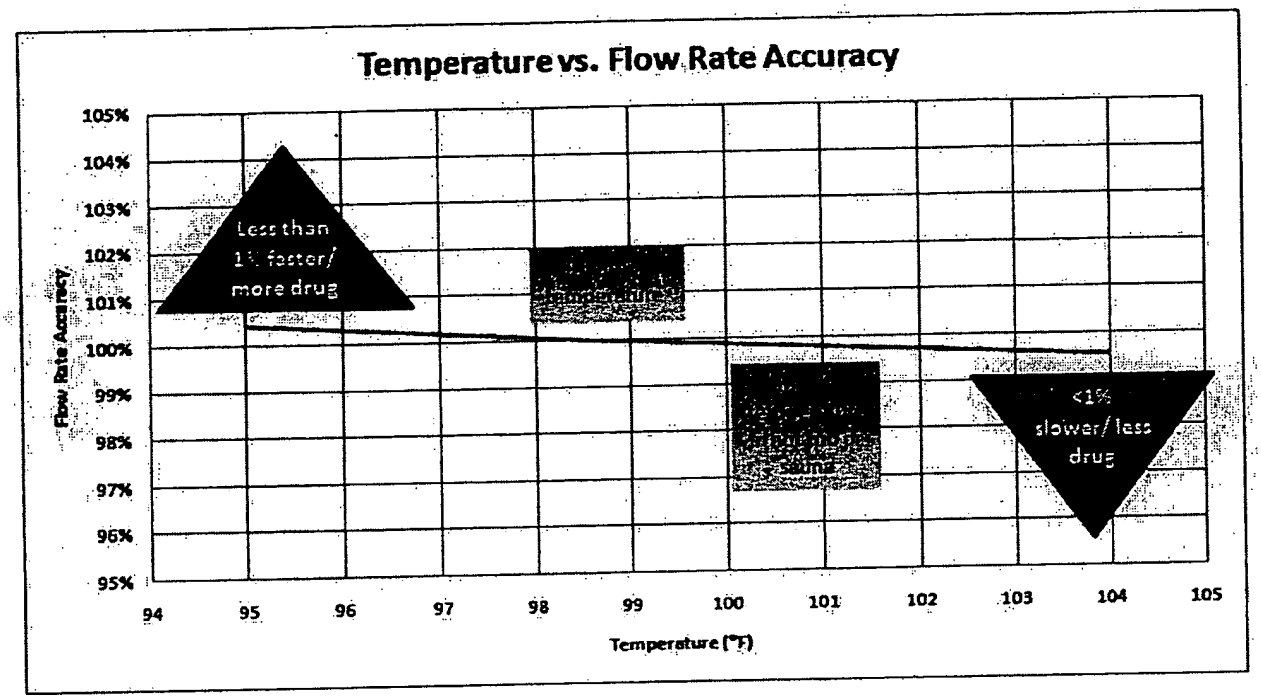
Activities such as scuba diving or hyperbaric therapy may cause the pump to temporarily stop delivering drug. When you return to normal atmospheric pressure, your pump will resume its programmed drug delivery. Discuss these activities with your doctor to see if you can safely be without your drug during scuba diving or hyperbaric therapy.

Do temperature changes affect my pump?

The Prometra programmable pump has a special design which isolates the drug reservoir from most temperature changes, making it ***immune to most temperature changes***. You are free to enjoy, with your doctor's permission:

- Hot tubs
- Whirlpool baths
- Saunas

These activities are SAFE and WILL NOT AFFECT YOUR PUMP. Always consult your doctor first about any other therapies not listed here.



Even temperature-related therapies such as deep heat therapy, e.g. diathermy, will not affect the operation of the pump. Always consult your doctor first about any other activities not listed here.

Can I travel with my pump?

The Prometra programmable pump provides you with the freedom to travel. Let your doctor know if you plan to travel so that pump refill arrangements can be made, if necessary. Also, your doctor can advise you of a doctor in the area you are traveling to in case you have any problems.

What should I do if I move?

Contact your doctor to ask for help finding a new pump management physician who can perform your refills. Then, when you have your new address, please contact **Customer Care** at **973-426-9229** so we can update our database in case we need to contact you.

Who do I need to tell about my pump and catheter implant?

You need to tell all medical personnel about your implant. This includes doctors, nurses and medical technicians, such as MRI or X-ray technicians. Knowing about the implant may change their treatment or how they conduct or interpret a medical test. To make this easy for you, you will receive an implant card that contains important information about your Prometra programmable pump and intrathecal catheter. Your implant card should be carried with you at all times.

What do I do if I have a question or suspect a problem?

If it is an emergency, always call 911. If you have pain, fever, chills, shortness of breath or dizziness, contact your doctor immediately. Also, if your pain increases or worsens, contact your doctor immediately. If you have any questions or suspect a problem, please contact your implanting or pump management doctor immediately.

Clinical Studies

The performance and safety of the Prometra Pump was examined in an open-label, non-randomized, multi-center study. This study was designed to demonstrate the accuracy and safety of the pump's delivery of Infumorph into the intrathecal space.

The goal of the study was to demonstrate accuracy of drug delivery is within the range of 85-115% through six months post implantation. Additionally the safety profile was evaluated, as determined by the rate of device-related serious adverse events and device complications.

A total of 110 Patients enrolled in the study were implanted with the Prometra Pump. Patients eligible for enrollment were suffering from cancer pain requiring strong opioids, chronic, non-malignant pain, or required an implantable pump system replacement due to malfunction or battery depletion.

Patients were followed monthly for the first 6 months post implantation. During each monthly follow-up visit, the pump was refilled and infused volumes of medication were documented. Drug delivery accuracy and adverse events were documented at the monthly visits.

Results

The goal of the study was achieved. The accuracy of drug delivery was found to be 96.8% with a 90% confidence interval of 95.5% - 97.7%. This met the required range of 85% - 115%.

Adverse Events reported during the study are shown in Table 1.

Table 1: Adverse Events Reported as Possibly, Probably, or Definitely Related to the Device or Study Procedure

System Organ Class	Preferred Term	N (%)
Gastrointestinal Disorders	Nausea	15 (14)
	Vomiting	8 (7)
General Disorders and Administration Site Conditions	Implant Site Pain	20 (18)
	Implant Site edema	11 (10)
	Implant Site Erythema (redness)	9 (8)
	Implant Site Swelling	4 (4)
	Pain	4 (4)

System Organ Class	Preferred Term	N (%)
	Implant Site Inflammation	3 (3)
	Drug Withdrawal Syndrome	2 (2)
	Implant Site Haemorrhage	2 (2)
	Pyrexia (fever)	2 (2)
	Tenderness	2 (2)
Infections and Infestations	Incision Site Infection	4 (4)
Injury, Poisoning and Procedural Complications	Procedural Pain	37 (34)
	Post Lumbar Puncture Syndrome	9 (8)
	Wound Secretion	9 (8)
	Seroma (pocket of fluid)	4 (4)
	Wound Dehiscence (re-opening)	3 (3)
Musculoskeletal and Connective Tissue Disorders	Back Pain	2 (2)
	Pain in Extremity	2 (2)
Nervous System Disorders	Headache	8 (7)
	Dizziness	3 (3)
	Intracranial Hypotension	2 (2)
Skin and Subcutaneous Tissue Disorders	Dermatitis Contact	5 (5)
	Pruritus (itching)	2 (2)
	Scab	2 (2)
Surgical and Medical Procedures	Surgery[1]	10 (9)

[1] Surgery to replace or revise intrathecal catheter

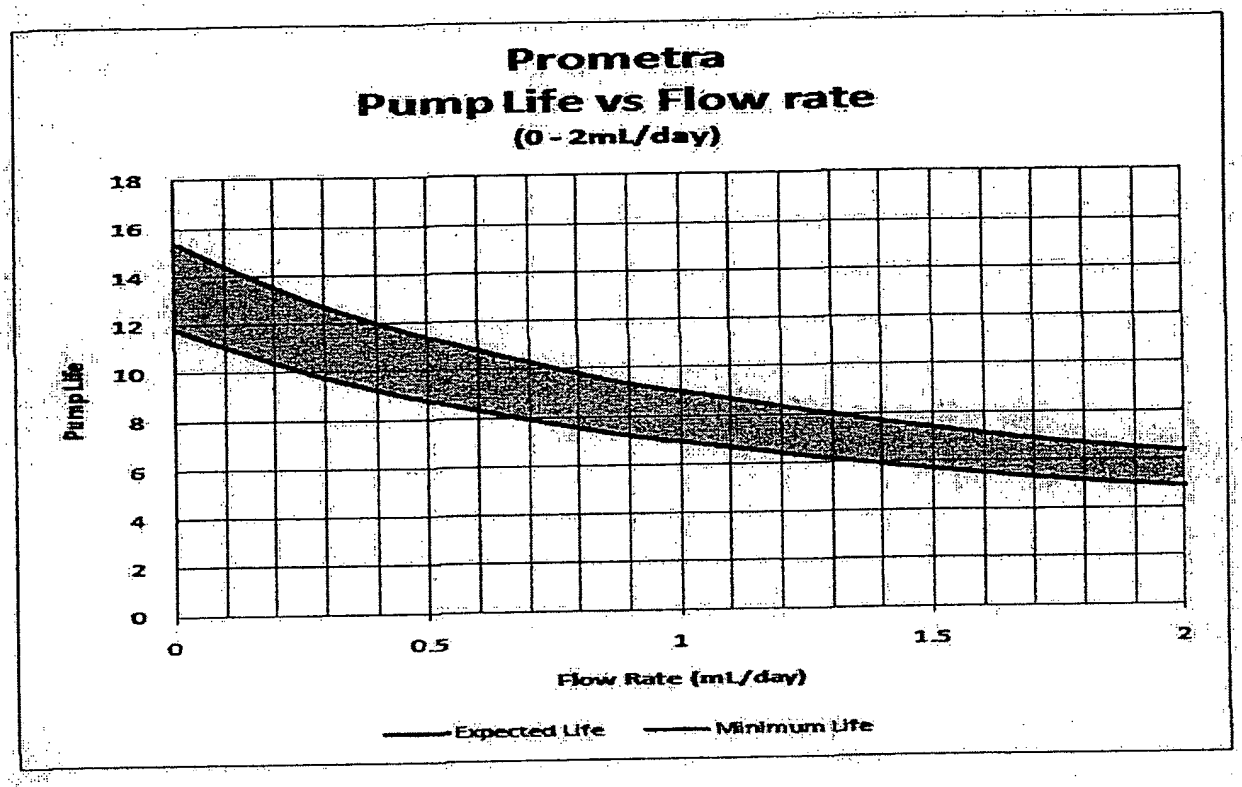
Adverse Events with incidence of 1% or less. Tinnitus (ringing in the ears), Abdominal Pain, Constipation, Oral Mucosal Blistering, Catheter Site edema, Implant Site Bruising, Implant Site Effusion, Implant Site Hypersensitivity, Implant Site Irritation, Implant Site Necrosis, Edema Peripheral, Hypersensitivity, Extradural Abscess, Implant Site Cellulitis (infection), Spinal Infection Viral, Excoriation, Hip Fracture[2], Procedural Nausea, Balance Disorder, Burning Sensation, Diplegia (paralysis), Hypoaesthesia (loss of feeling), Neuropathy Peripheral (Nerve impairment), Tremor, Dyspnoea (shortness of breath), Respiratory Depression, Ecchymosis (bruise), Rash, Haematoma.

[2]Event occurred while patient was being treated with a drug other than Infumorph via Prometra System

Operating Information

Expected Pump Life

The Prometra programmable pump has a battery which powers the pump. The normal battery life of the pump is a minimum of 10 years at a drug delivery rate of 0.25 mL/day. If you receive a higher flow rate, your battery life may be less. If you receive a lower flow rate, your pump battery should last longer. The below chart will give you an idea of your pump life. If you have any questions, please ask your implanting doctor or pump management doctor.



The only way you can monitor the activity of your Prometra programmable pump system is by keeping track of how well your symptoms are controlled. Please keep a diary or other daily record of your symptom levels, noting your activities immediately preceding an increase or decrease in symptoms. Set aside time to regularly discuss your daily record with your doctor or refill nurse. Taking an active role in your care will help you to achieve the best symptom control.

Instructions on how to safely dispose of the device

The pump can be removed by your doctor in a surgical procedure like the one that was used to put the pump into your body. Once your pump is explanted, it will be returned to Medasys for proper disposal.

The pump will need to be explanted upon your death. If you are terminally ill, please notify your caregiver and primary doctor that the pump may explode during cremation and needs to be removed prior to cremation or burial.

Additional Information

Warranty

Medasys, Inc. ("Medasys") warrants to the first purchaser of this product that this product will be free from defects in materials and workmanship for a period of one year from the date of first purchase, and liability under this limited product warranty will be limited to repairing or replacing the defective product, at Medasys' sole discretion, or refunding the net price paid. Wear and tear from normal use or defects resulting from misuse of this product is not covered by this limited warranty.

TO THE EXTENT ALLOWABLE BY APPLICABLE LAW, THIS LIMITED PRODUCT WARRANTY IS IN LIEU OF ALL OTHER WARRANTIES, WHETHER EXPRESS OR IMPLIED, INCLUDING, BUT NOT LIMITED TO, ANY IMPLIED WARRANTY OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE. IN NO EVENT WILL MEDASYS BE LIABLE TO YOU FOR ANY INCIDENTAL OR CONSEQUENTIAL DAMAGES RESULTING FROM YOUR HANDLING OR USE OF THIS PRODUCT.

Some states/countries do not allow an exclusion of implied warranties, or incidental or consequential damages. You may be entitled to additional remedies under the laws of your state/country.

Travel or international use

There are no restrictions on travel. However, you will want to arrange with your doctor in advance to obtain the name of a local pump management doctor in case of emergency or prolonged vacation requiring a refill.

Date of Version

January 2012.

User Assistance Information

Please contact us with any questions or comments via either phone, email or the web. We always welcome patient input.

- 973.426.9229
- customercare@medasyspumps.com
- medasyspumps.com

If you wish to write to us, we would love to hear from you. Here is our address:

Medasys Inc.
500 International Drive, Suite 200
Mount Olive, NJ 07828 USA
T 973.426.9229
F 973.426.0035

Manufactured for:
Medasys Inc.
500 International Drive, Suite 200
Mount Olive, NJ 07828 USA
T 973.426.9229
F 973.426.0035
medasyspumps.com

PL-01912-05

MEDASYS™
Implanting Confidence

Unsafe near
strong magnets

Patient Implant Card

Prometra® Programmable Pump & Intrathecal Catheter

Your pump may trigger airport metal detectors.

If you move or change doctors, please immediately notify Customer Care at 973.426.9229.

In case of emergency, call 911.

If you are concerned about any changes or symptoms that may relate to the pump, contact your implanting physician immediately.

Unsafe near
strong magnets

Medasys Inc.
500 International Drive, Suite 200
Mount Olive, NJ 07828 USA
T 973.426.9229
F 973.426.0035
www.MedasysPumps.com

PL-02375-06

Patient Name: _____

Implanting Physician: _____

Phone: _____

Pump Volume: 20 mL Pump Location: _____

Catheter Length Implanted: _____ Catheter Volume: _____

Catheter Tip Location: _____

WARNING: Patients should not undergo MRI or other magnetic therapies. Failure to empty the pump prior to exposure to MRI environment could result in drug overdose that could lead to serious patient injury or death.

Caution, consult accompanying documents.

Use only products labeled for use with Prometra pumps to refill or access this pump.

Date Implanted: Month Day Year

Place Catheter Sticker Here

Place Pump Sticker Here

MEDASYS
Implanting Confidence

Unsafe near strong magnets

Patient Implant Card

Prometra® Programmable Pump & Intrathecal Catheter

Your pump may trigger airport metal detectors.

If you are concerned about any changes or symptoms that may relate to the pump, contact your implanting physician immediately.

If you move or change doctors, please immediately notify Customer Care at 973.426.9229.

www.MedasysPumps.com
Mount Olive, New Jersey (USA)

PL-02300-04

Patient:

	Model	Serial/Lot	Implant Date	Volume
Pump				
Catheter				

Pump Location:

Catheter Tip Location:

Catheter Length Implanted:

Implanting Physician:

Phone:

WARNING: Patients should not undergo MRI or other magnetic therapies. Failure to empty the pump prior to exposure to MRI environment could result in drug overdose that could lead to serious patient injury or death.

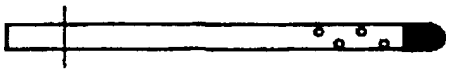
⚠ Caution, consult accompanying documents.

Use only products labeled for use with Prometra pumps to refill or access this pump.

MEDASYS™
Implanting Confidence™

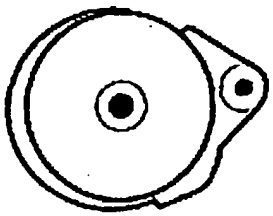
INTRATHECAL CATHETER

For use with Prometra® Programmable Pump



PROMETRA® PROGRAMMABLE PUMP

For use with Intrathecal Catheter



Caution: Federal Law (USA) restricts this device to sale by or on the order of a physician.

Contents

Introduction

The Prometra Programmable Pump is designed to provide controlled delivery of Infumorph® to the intrathecal space via the separately supplied Intrathecal Catheter. The Prometra Programmer is a separately supplied handheld, menu-driven device that enables remote programming of the Prometra Pump.

Note: The use of the terms "medication" and "drug" throughout this document refer to the use of Infumorph.

Contents

Catheter Contents

The following components are sterile and non-pyrogenic:

1 - Catheter, Radiopaque, 1.3 mm OD (4F) x 110 cm x 0.6 mm ID
1 - Catheter Lock
1 - Hub, Flushing, 0.6 mm (23G) x 13 mm (0.5 in.)
1 - Needle, Tuohy, 1.8 mm (15G) x 89 mm (3.5 in.)
1 - Stylet, Hydrophilic, Flush-Through, 0.43 mm (0.017 in.) x 109 cm
1 - Syringe, 12 mL, Luer Slip
2 - Wings, Suture, 90°, Angled with:
  2 – Anchors, Angled
1 Wing, Suture, Slit with:
  1 – Anchor, Straight

Non-sterile components:

1 – Patient and Physician Information Packet:
  1 – Instructions for Use
  1 – Calculations Guide
  1 – Patient Guide
  2 – Temporary Patient Implant Cards
  1 – Sheet of Device ID Stickers
  1 – Patient Device Tracking Form

Pump Contents

The following components are sterile and non-pyrogenic:

1 – Prometra Programmable Pump
1 – Needle, Non-Coring, 0.7 mm (22G) x 38 mm (1.5 in.)
1 – Needle, Catheter Access, 0.9 mm (20G) x 45 mm (1.75 in.)

Non-sterile components:

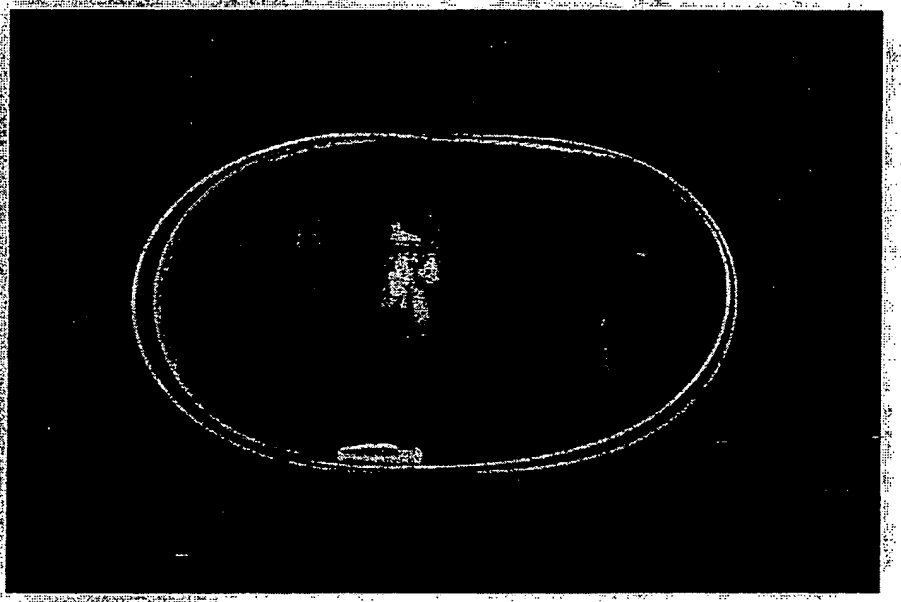
1 – Patient and Physician Information Packet:
  1 – Instructions for Use
  1 – Calculations Guide
  1 – Patient Guide
  2 – Temporary Patient Implant Cards

1 – Sheet of Device ID Stickers
1 – Patient Device Tracking Form

Description

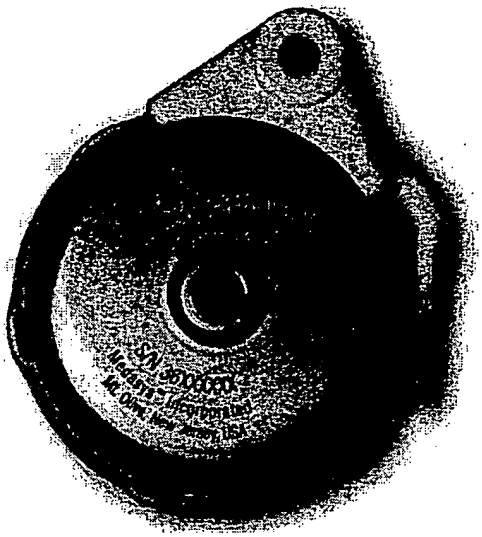
Catheter Description

The Intrathecal Catheter is a single-piece, radiopaque, silicone catheter with pre-inserted hydrophilic stiffening stylet that is used to assist in placing the catheter. The catheter has a tungsten-filled tip to enhance radiopacity and side-holes at the tip for dispersion of the infusate into the intrathecal space. The catheter also features depth markings indicated in centimeters starting 5 cm from the distal end of the catheter, extending to a distance 30 cm from its distal end. The intrathecal catheter is provided with accessories to assist in its placement and fixation at implant and a radiopaque catheter lock to connect the catheter to the Prometra Programmable Pump.



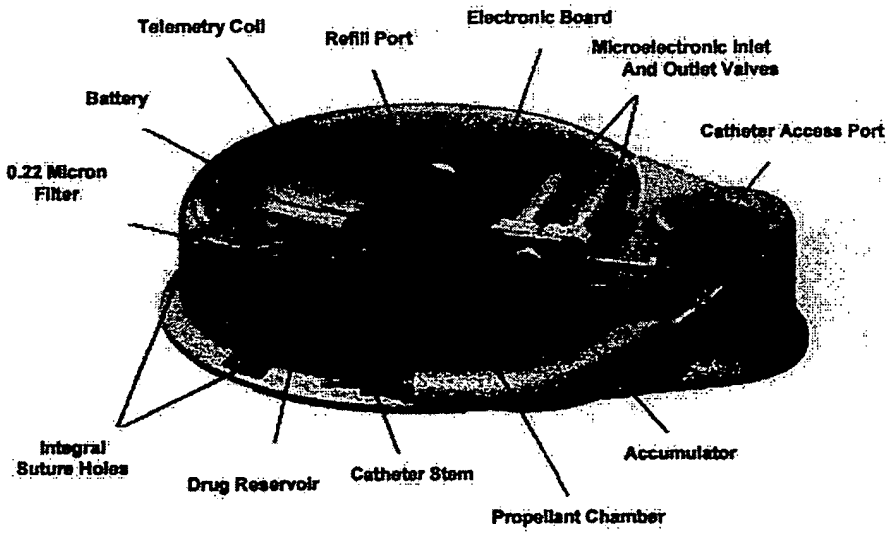
Pump Description

The Prometra Pump is a battery-powered, teardrop-shaped pump with a rigid titanium housing and a triple redundancy flow controller system.



The triple redundancy flow control system is designed to provide a precise and accurate flow rate. The flow rate accuracy is independent of normal operating environmental conditions such as altitude, temperature and reservoir volume.

Once implanted, the device can be identified by using the programmer to inquire the system. If a programmer is not available, the shape of the pump, tear drop access port and raised refill port provide features distinct to the Prometra pump for easy identification.



Specifications of the Prometra Programmable Pump are:

Device Longevity	
Pump	10 years at 0.25 mL/day
Septum (Refill and CAP)	1000 punctures maximum
External Properties	
Material	Titanium Polyphenylsulfone access ports
Thickness (nominal)	20 mm
Diameter (excluding CAP)	69 mm
Average Volume Displacement	100 mL
Weight, unfilled	150 g
Drug Reservoir	
Material	Titanium
Usable Capacity	20 mL
Precision Dosing System	
Material	Titanium MP35N alloy Stainless steel Silicone rubber
Refill Septum	
Septum material	Silicone rubber
Access needle	Huber point, 22G non-coring needle
Catheter Access Septum	
Septum material	Silicone rubber
Access needle	Lancet point with side hole, 20G
Bacterial filter	
Material	Polyvinylidene fluoride
Pore size	0.22 micron
Flow Rate	
Range	0-28.8 mL/day
Accuracy	95.9-97.7% (90% confidence limit)
Refill Interval	Not more than 90 days

The pump is supplied with a Catheter Access needle and a non-coring Refill needle for priming the pump at implantation. The Patient Information packet contains a patient guide and two patient

implant cards to be completed and given to the patient. Additionally, a federally-mandated patient device tracking form is included.

Indications

The Prometra Programmable Infusion System is indicated for intrathecal infusion of Infumorph® (preservative-free morphine sulfate sterile solution) or preservative-free sterile 0.9% saline solution (Sodium Chloride Injection, USP).

Drug Information

Refer to the Infumorph labeling for a complete list of indications, contraindications, warnings, precautions, dosage administration information and screening procedures

Contraindications

Implantation of this device is contraindicated when:

- The presence of infection is known or suspected.
- The patient's body size or anatomy is insufficient to accommodate the size of the implanted pump or catheter.
- The pump cannot be implanted 2.5 cm (1 in.) or less from the surface of the skin. Deeper implants could interfere with septum access or telemetry.
- The patient is known or is suspected to be allergic to materials contained in the catheter: silicone elastomers, barium sulfate, tungsten, polyacetal resin, ink, stainless steel, hydroglide hydro gel coating, or plastic needle hubs (polypropylene and acrylic based).
- The patient is known or is suspected to be allergic to materials contained in the pump: titanium, silicone elastomers, polyphenylsulfone, silicone adhesive, polyvinylidene fluoride, MP35N metal (nickel-cobalt-chromium-molybdenum alloy), or stainless steel (AL29-4, 316L).
- The patient has exhibited a prior intolerance to implanted devices.
- The patient has a spinal column anatomy that would obstruct cerebrospinal fluid flow or that would prevent intraspinal drug administration.
- The patient has emotional, psychiatric or substance abuse problems that are deemed to prohibit intrathecal drug administration.
- Contraindications relating to Infumorph must be observed and followed per the approved drug labeling.

Warnings

General

WARNING: USE OF UNAPPROVED DRUGS (e.g., DRUG COCKTAILS, PHARMACY-COMPOUNDED DRUGS, MORPHINE WITH PRESERVATIVES, ETC.) WITH THE PROMETRA PUMP COULD RESULT IN PUMP FAILURE AND/OR SERIOUS ADVERSE EVENTS INCLUDING DEATH.

WARNING: PATIENTS SHOULD NOT UNDERGO MRI OR OTHER MAGNETIC THERAPIES. FAILURE TO EMPTY THE PUMP PRIOR TO EXPOSURE TO MRI ENVIRONMENT COULD RESULT IN DRUG OVERDOSE THAT COULD LEAD TO SERIOUS PATIENT INJURY OR DEATH.

- Prior to infusion of Infumorph into the catheter, medical personnel should be familiar with and observe all warnings, cautions, contraindications, and instructions as specified by the drug manufacturer.
- Patients should not undergo hyperbaric therapy since exposure could result in drug underdose.
- Always select and program dosages consistent with the Infumorph® labeling to prevent improper drug administration.
- In the event of over-medication, refer to the approved Infumorph labeling for appropriate treatment.
- *Clinicians implanting, programming,* accessing, or maintaining implanted programmable pumps must comply with the instructions for use. Technical errors may result in a return of underlying symptoms, drug withdrawal symptoms, or clinically significant or fatal overdose.
- The Intrathecal Catheter and Prometra Programmable Pump components are supplied sterile and non-pyrogenic. The packages should be examined carefully prior to opening. Do not use the contents if there is any evidence of damage to the package or package seal that could compromise sterility. Do not resterilize contents of any damaged or opened packages.
- After use, this device is a biohazard. Handle and dispose of in accordance with accepted hospital practice and all applicable laws and regulations.
- Do not incinerate or cremate the pump.
- Do not expose the pump to temperatures above 57°C (134.6°F) or below 2°C (35.6°F).
- The patient has an occupation where he/she would be exposed to high current industrial equipment, powerful magnets or transmitting towers, such as, electricians, electrical engineers or MRI technicians.

Preparation for MRI Procedure

IF AN MRI PROCEDURE IS NECESSARY, THE PUMP MUST BE EMPTIED of drug solution, not refilled and the PUMP PROGRAMMED TO 0.0 ML DRUG FLOW RATE prior to entering the environment of the MRI. FAILURE TO EMPTY THE PUMP PRIOR TO EXPOSURE TO MRI ENVIRONMENT COULD RESULT IN SERIOUS PATIENT INJURY OR DEATH.

Prior to initiating the MRI procedure, the physician should determine if the patient could safely be deprived of pain medication for the length of the procedure. If pain medication is needed, then alternate means of drug delivery (such as I.V. administration) should be employed for the duration of the MRI procedure.

THE PUMP CANNOT BE USED AFTER EXPOSURE TO MRI.

IF AN MRI PROCEDURE HAS BEEN UTILIZED THE PUMP SHOULD BE EXPLANTED.

Precautions

General

- Carefully read all instructions prior to use. Follow all instructions.
- Certain equipment may cause electrical noise, which may interfere with programming. If suspected, move the patient from the suspected source of interference to facilitate the programming procedure. Examples of equipment that may cause interference include cathode ray tube (CRT) monitors and large electric motors.
- Do not use accessories that are not referenced in these instructions for use. Only use devices and accessories that are referenced for use with the Prometra® Programmable Pump in these instructions.
- Safety and effectiveness for use in pediatric patients under 22 years old has not been investigated or established.
- The effects of implanting this device in patients with other implanted medical devices, other than neurostimulators, are unknown.
- Pain on injection that was not noted during previous injections may be an early sign of infection.

Implant

- Implantation of this device and subsequent use, reprogramming, and refill should only be conducted by qualified medical personnel specifically trained for surgical implantation, use, and maintenance of the device. Use of this device by non-qualified or untrained personnel could lead to serious consequences involving under- or over-dosage of Infumorph. In the event of over-dosage , refer to the approved Infumorph labeling for appropriate treatment.
- The pump and catheter system should be implanted carefully to avoid any sharp or acute angles, which could compromise the patency of the catheter lumen.
- Over-pressurization can damage the catheter. Small syringes can generate very high pressures and may damage the catheter or catheter connection. Do not use a syringe smaller than 10 mL when accessing the catheter access chamber.
- If therapy is discontinued for an extended period, the pump should be emptied of Infumorph and filled with a preservative-free 0.9% sterile saline solution and programmed to a low infusion rate to maintain catheter patency.

Device Compatibility

- **Pump accessories.** Only use the Prometra Programmable Pump with the accessories listed in these instructions for use. Use of alternate accessories may result in damage to Prometra components, less than adequate therapy, or increased risks to the patient.
- **Pump.** Only use with Prometra Programmer.
- **Alcohol.** Do not use alcohol on any part of the pump or catheter system. Alcohol is neurotoxic.
- **Contrast media.** Do not inject contrast media into the refill reservoir since this may damage the pump or impair pump function.
- **External devices.** Do not connect any external devices or pumps to the Prometra Pump. Pressures generated by an external pump could damage the implanted pump/catheter system and result in serious patient injury or death.
- **Therapeutic ultrasonics or lithotripsy** - Use of therapeutic ultrasonic devices, such as

electrohydraulic lithotriptors, has not been tested on the Prometra pump. If lithotripsy must be used, do not focus the beam in proximity of the pump.

- ***Medical devices.*** *The Prometra Pump Programmer may affect other medical devices. Use or interference with medical devices, other than neurostimulators, has not been established.*
- **Applied electric currents.** Interaction of the Prometra Pump with electric currents applied to the body such as cardioversion or defibrillation has not been established. Care must be exercised if the patient receives these treatments. Where practical, the pump should be turned off before application of electric currents to the patient's body. Confirmation that the pump programming has not changed must be carried out as soon as possible after the procedure.
- **Radiation.** Do not use radiation therapy in the area of the pump. The effects of ionizing radiation on the Prometra Pump have not been established, and these therapies may have effects on pump operation that are not immediately apparent.

Potential Adverse Events

The use of implanted pumps provides an important means of intrathecally delivering Infumorph. However, the potential exists for serious complications including the following:

Possible Risks Associated with Programmable Implantable Pump:

- Adverse reaction to pump materials
- Battery depletion
- Bleeding
- Body rejection phenomena
- Defective pump (e.g. propellant chamber leakage, pump rupture)
- Inability to locate septum
- Inability to program pump due to programmer failure or loss of telemetry
- Inflammation, necrosis, or scarring of skin over implant area
- Programming errors, resulting in over or under dosing
- Pump flipping or twisting
- Pump implanted too deep, resulting in difficulty accessing or inability to access port
- Pump migration
- Pump pocket pain/soreness
- Pump pocket seroma/hematoma, with or without infection
- Pump rotation
- Pump site skin erosion
- Pump stoppage
- Refill errors, including injection into pump pocket, injection into wrong port, incorrect volume, incorrect concentration, difficulty accessing pump port
- Septum dislodgement
- Septum leakage
- Slow, erratic or fast flow
- Software error

Possible Risks Associated with Intrathecal Catheter:

- Catheter disconnection
- Catheter kinking
- Catheter fracture
- Catheter migration (unrelated to surgical complication)
- Cerebrospinal fluid (CSF) leak
- Disconnection
- Erosion
- Fibrosis
- Infection in intrathecal space, including meningitis
- Inflammatory mass formation (e.g., granuloma)
- Malpositioning
- Nerve damage
- Pain on injection
- Poor radiopacity
- Post dural puncture headache
- Reaction to catheter materials
- Reversible or irreversible partial or complete occlusions
- Spinal cord pressure leading to paralysis
- Spinal cord trauma, perforation, laceration
- Subcutaneous catheter tract infection
- Subcutaneous tunnel infection
- Tears/breaks

In rare instances, the development of an inflammatory mass at the tip of the implanted catheter may occur, which can result in serious neurological impairment. Patients should be monitored carefully at each visit for any new neurological signs or symptoms, including:

- progressive change in the character, quality, or intensity of pain
- an increase in the level and degree of pain despite dose escalation
- sensory changes (i.e., numbness, tingling, burning)
- hyperesthesia and/or hyperalgesa

Presentations that require immediate diagnosis include

- bowel and/or bladder dysfunction
- myelopathy
- conud syndrome
- gait disturbances or difficulty ambulating
- paraparesis or paralysis

If the presence of an inflammatory mass is suspected, recommended evaluation should include a review of the patient history and neurological evaluation, radiological diagnostic procedures (such as a CT scan with contrast) and appropriate clinical consultation.

Inflammatory mass has been associated with a wide range of doses and concentrations of opioids. No dose or concentration of Infumorph can be considered completely free of risk from inflammatory

mass. The risk of inflammatory mass occurrence appears to be cumulative over time and increases with higher concentrations and doses of opioids.

Clinical Studies

The performance and safety of the Prometra Pump was examined in an open-label, non-randomized, multi-center study. This study was designed to demonstrate the accuracy and safety of the pump's delivery of Infumorph into the intrathecal space.

The primary endpoint of the study was to demonstrate accuracy of drug delivery is within the range of 85-115% through six months post implantation. Additional endpoints evaluated the safety profile, as determined by the rate of device-related serious adverse events and device complications.

A total of 110 Patients enrolled in the study were implanted with the Prometra Pump. Patients eligible for enrollment were suffering from cancer pain requiring strong opioids, chronic, non-malignant pain, or required an implantable pump system replacement due to malfunction or battery depletion. The average patient age at implant was 56 years with 54% male and 46% female patients.

Patients were followed monthly for the first 6 months post implantation. During each monthly follow-up visit, the pump was refilled and infused volumes of medication were documented. Drug delivery accuracy and adverse events were documented at the monthly visits.

Results

The accuracy of drug delivery was found to be 96.8% with a 90% confidence interval of 95.5% - 97.7%. This met the required range of 85% - 115%.

Adverse Events reported during the study are shown in Table 1.

Table 1: Adverse Events Reported as Possibly, Probably, or Definitely Related to the Device or Study Procedure

System Organ Class	Preferred Term	N (%)
Gastrointestinal Disorders	Nausea	15 (14)
	Vomiting	8 (7)
General Disorders and Administration Site Conditions	Implant Site Pain	20 (18)
	Implant Site edema	11 (10)
	Implant Site Erythema	9 (8)
	Implant Site Swelling	4 (4)

System Organ Class	Preferred Term	N (%)
	Pain	4 (4)
	Implant Site Inflammation	3 (3)
	Drug Withdrawal Syndrome	2 (2)
	Implant Site Haemorrhage	2 (2)
	Pyrexia	2 (2)
	Tenderness	2 (2)
Infections and Infestations	Incision Site Infection	4 (4)
Injury, Poisoning and Procedural Complications	Procedural Pain	37 (34)
	Post Lumbar Puncture Syndrome	9 (8)
	Wound Secretion	9 (8)
	Seroma	4 (4)
	Wound Dehiscence	3 (3)
Musculoskeletal and Connective Tissue Disorders	Back Pain	2 (2)
	Pain in Extremity	2 (2)
Nervous System Disorders	Headache	8 (7)
	Dizziness	3 (3)
	Intracranial Hypotension	2 (2)
Skin and Subcutaneous Tissue Disorders	Dermatitis Contact	5 (5)
	Pruritus	2 (2)
	Scab	2 (2)
Surgical and Medical Procedures	Surgery[1]	10 (9)

[1] Surgery to replace or revise intrathecal catheter

Adverse Events with incidence of 1% or less. Tinnitus, Abdominal Pain, Constipation, Oral Mucosal Blistering, Catheter Site Edema, Implant Site Bruising, Implant Site Effusion, Implant Site Hypersensitivity, Implant Site Irritation, Implant Site Necrosis, Edema Peripheral, Hypersensitivity, Extradural Abscess, Implant Site Cellulitis, Spinal Infection Viral, Excoriation, Hip Fracture[2], Procedural Nausea, Balance Disorder, Burning Sensation, Diplegia, Hypoaesthesia, Neuropathy Peripheral, Tremor, Dyspnoea, Respiratory Depression, Ecchymosis, Rash, Haematoma.

[2]Event occurred while patient was being treated with a drug other than Infumorph via Prometra System

Equipment

- Prometra Programmable Pump
- Intrathecal Catheter
- Tunneler
- Prometra Pump Programmer (Not Sterile)

The following items may be needed and are not provided:

- Sterile Programmer Sleeve
- Sterile preservative-free 0.9% saline
- Infumorph solution (infusate) for refill, not to exceed 20 mL

SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name:	Implantable Infusion Pump
Device Trade Name:	Prometra® Programmable Infusion Pump System
Applicant's Name and Address:	Medasys, Inc. 500 International Drive, Suite 200 Mount Olive, NJ 07828
Date of Panel Recommendation:	None
PMA Number:	P080012
Date of Notice of Approval:	February 7, 2012
Expedited:	Not Applicable

II. INDICATIONS FOR USE

The Prometra® Programmable Infusion Pump System is indicated for intrathecal infusion of Infumorph (preservative-free morphine sulfate sterile solution) or preservative-free sterile 0.9% saline solution (Sodium Chloride Injection, USP).

III. CONTRAINDICATIONS

Implantation of this device is contraindicated when:

a. The presence of infection is known or suspected.

b. The patient's body size or anatomy is insufficient to accommodate the size of the implanted pump or catheter.

c. The pump cannot be implanted 1 in. (2.5 cm) or less from the surface of the skin. Deeper implants could interfere with septum access or telemetry.

d. The patient is known or is suspected to be allergic to materials contained in the catheter: silicone elastomers, barium sulfate, tungsten, polyacetal resin, ink, stainless steel, hydroglide hydro gel coating, or plastic needle hubs (polypropylene and acrylic based).

e. The patient is known or is suspected to be allergic to materials contained in the pump: titanium, silicone elastomers, polyphenylsulfone, silicone adhesive, polyvinylidene fluoride, MP35N metal (nickel-cobalt-chromium-molybdenum alloy), or stainless steel (AL29-4, 316L).

f. The patient has exhibited a prior intolerance to implanted devices.

g. The patient has a spinal column anatomy that would obstruct good cerebrospinal fluid flow or that would prevent intraspinal drug administration.

h. The patient has emotional, psychiatric or substance abuse problems that are deemed to prohibit intrathecal drug administration.

i. Contraindications relating to Infumorph must be observed and followed per the approved drug labeling.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Prometra® Programmable Infusion Pump System labeling.

Warnings and precautions relating to Infumorph must be observed and followed per the approved drug labeling.

V. DEVICE DESCRIPTION

The Prometra Implantable Pump components consist of the following devices:

- Prometra Programmable Pump
- Intrathecal Catheter

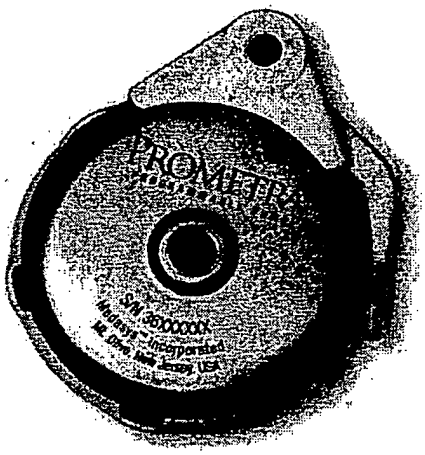
The Prometra Implantable Pump accessories consist of the following:

- Prometra Programmer
- Tunneler
- Refill Kit
- Catheter Access Port (CAP) Kit

Prometra Programmable Pump

The Prometra Programmable Pump is a sterile, battery-operated, teardrop-shaped implantable, programmable infusion pump, with a rigid titanium housing and triple redundancy flow controller system, that dispenses Infumorph into the intrathecal space through an implanted infusion catheter. All functions of the system (e.g., dosing) are controlled externally using a hand-held, battery-operated programmer. The Prometra Pump (FIGURE 1) contains a metal bellows drug reservoir with a capacity of 20 milliliters (mL). The reservoir propellant is stored within the rigid housing surrounding the bellows and provides the driving pressure for the pump. The driving pressure on the reservoir forces the Infumorph through an outlet filter (0.22 μm), and into an electronically controlled flow metering valve-accumulator subsystem. The Infumorph passes from the flow metering subsystem, into the catheter access port then into the catheter for delivery to the intrathecal space. The specifications of the Prometra Pump are listed in Table 1.

9



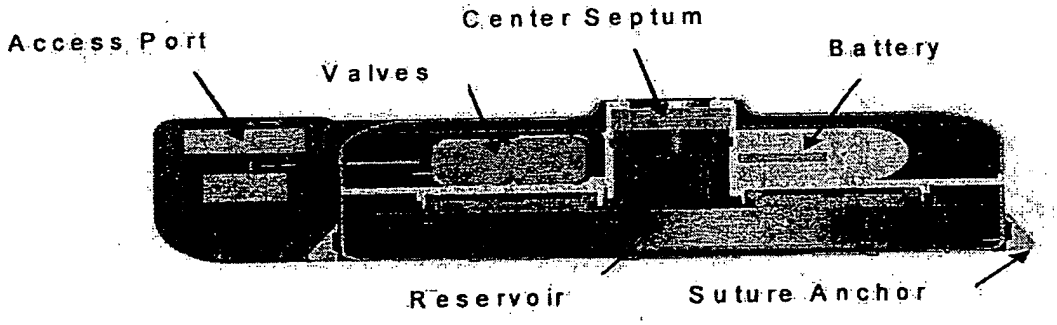


FIGURE 1: Prometra Pump

Table 1 – Specifications of the Prometra Programmable Pump

Device Longevity	
Pump	10 years at 0.25 mL/day
Septum (Refill and CAP)	1000 punctures maximum
External Properties	
Material	TitaniumPolyphenylsulfone access ports
Thickness (nominal)	20 mm
Diameter (excluding CAP)	69 mm
Average Volume Displacement	100 mL
Weight, unfilled	150 g
Drug Reservoir	
Material	Titanium
Usable Capacity	20 mL

Precision Dosing System	
Dose Dispenser Volume	2 mcL
Material	Titanium, MP35N alloy, Stainless steel, and Silicone rubber
Refill Septum	
Septum material	Silicone rubber
Access needle	Huber point, 22G non-coring needle
Catheter Access Septum	
Septum material	Silicone rubber
Access needle	Lancet point with side hole, 20G
Bacterial filter	
Material	Polyvinylidene fluoride
Pore size	0.22 micron
Flow Rate	
Range	0-28.8 mL/day
Accuracy	95.9-97.7% (90% confidence limit)
Refill Interval	No more than 90 days

Catheter

The Intrathecal Catheter (FIGURE 2) is a sterile, single-piece, radiopaque, silicone catheter with a pre-inserted hydrophilic stiffening stylet that is used to assist in placing the catheter. The catheter has a tungsten-filled tip to enhance radiopacity and side-holes at the tip for dispersion of the infusate into the intrathecal space. The catheter also features depth markings indicated in centimeters starting 5 cm from the distal end of the catheter, extending to a distance 30 cm from its distal end. The intrathecal catheter is provided with accessories to assist in its placement and to secure at implant. It has a radiopaque catheter lock to secure the catheter onto the stem of the Prometra Programmable Pump.

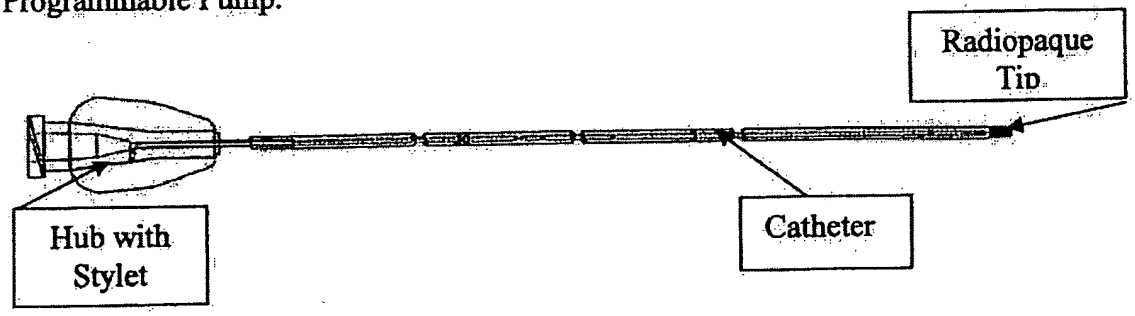


FIGURE 2: Medasys Intrathecal Catheter

Accessories

The accessories of the implantable components are limited to the programmer, tunneler, and kits which provide the necessary components for programming the pump, refilling the pump, and accessing the catheter via the catheter access port.

Programmer
The Prometra Programmable Pump is non-sterile and can be programmed with the Prometra Programmer (FIGURE 3) to deliver a precise flow of medication at a constant or variable rate, or it can be set to periodically deliver a drug dosage at distinct intervals of time (i.e., Periodic Flow Mode).

There is also an option to interrupt the pump's current medication regimen and deliver an immediate infusion of medication (Demand Bolus).

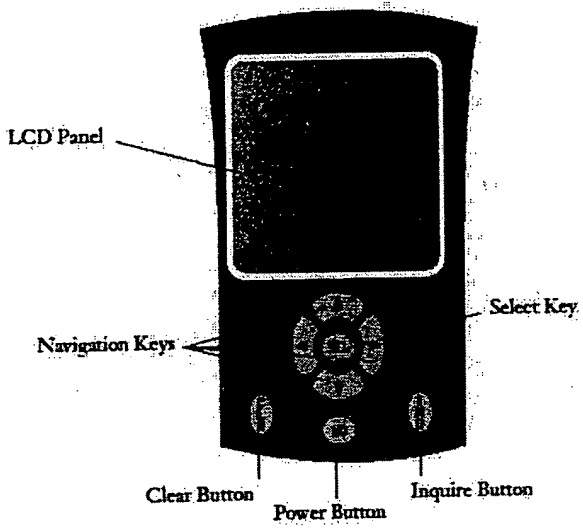


FIGURE 3: Prometra Programmer

Tunneler
The tunneler is used for subcutaneous placement of the Intrathecal Catheter. It is a sterile, malleable stainless steel tunneler with a pointed tip to penetrate subcutaneous tissue and a threaded end or attachment to the Intrathecal Catheter.

Refill Kit
The refill kit is sterile and provides the components and instructions necessary to access the pump reservoir to empty and fill the Prometra Programmable Pump. The refill kit includes:

2 - Adhesive Bandages, Round
1 - Calibrated Syringe Barrel, 12 mL
1 - Syringe Cap
1 - Stopcock
1 - CSR Wrap
1 - Extension Tubing, 20 cm (8 in.), with Clamp
1 - Fenestrated Drape
1 - Filter, 0.22 micron
4 - Gauze Pads, 10 cm x 10 cm, (4 in. x 4 in.)
2 - Non-Coring Needles, 0.7 mm (22G) x 38 mm (1.5 in.)
1 - Refill Template

Catheter Access Port Kit

The catheter access port kit is sterile and provides the components and instructions necessary to access the catheter access port of the Prometra Programmable Pump: The catheter access port kit includes:

2 - Adhesive Bandages, Round
1 - CSR Wrap
1 - Fenestrated Drape
1 - Extension Tubing, 20 cm (8 in.), with Clamp
1 - Filter, 0.22 micron
4 - Gauze Pads, 10 cm x 10 cm (4 in. x 4 in.)
1 - Needle, Catheter Access, 0.9 mm (20G) x 45 mm (1.75 in.)
1 - Syringe, 10 mL, Luer Lock
1 - Catheter Access Template

The drug chamber is refillable and is percutaneously accessed via the centrally-located access port using a 22-gauge non-coring needle. The catheter access port is located on the periphery of the pump to allow for direct access to the catheter without interfering with the drug reservoir. The catheter access port can be used to evaluate catheter patency or catheter placement.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternative forms of treatment with drugs including use in conventional routes of administration: oral, intramuscular, intravenous, percutaneous, transdermal; or treatment with other commercially available implantable infusion pumps. Other alternatives also include sympathetic nerve blocks, transcutaneous electrical nerve stimulation (TENS), spinal cord stimulation, anti-inflammatory agents, or steroids. Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with his/her physician to select the method that best meets expectations and lifestyle.

VII. MARKETING HISTORY

The Prometra® Programmable Infusion Pump System has not been marketed within the United States. The device has received marketing approval in the European Union. The device has not been withdrawn from marketing for any reason relating to the safety or effectiveness of the device.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of the potential adverse effects (or risks) related to the use of the pump and/or catheter includes, but is not limited to, the following conditions:

Possible Risks Associated with Programmable Implantable Pump

- Adverse reaction to pump materials
- Battery depletion
- Bleeding

- Body rejection phenomena
- Defective pump (e.g. propellant chamber leakage, pump rupture)
- Inability to locate septum
- Inability to program pump due to programmer failure or loss of telemetry
- Inflammation, necrosis, or scarring of skin over implant area
- Programming errors, resulting in over or under dosing
- Pump flipping or twisting
- Pump implanted too deep, resulting in difficulty accessing or inability to access port
- Pump migration
- Pump pocket pain/soreness
- Pump pocket seroma/hematoma, with or without infection
- Pump rotation
- Pump site skin erosion
- Pump stoppage
- Refill errors, including injection into pump pocket, injection into wrong port, incorrect volume, incorrect concentration, difficulty accessing pump port
- Septum dislodgement
- Septum leakage
- Slow, erratic or fast flow
- Software error

Possible Risks Associated with Intrathecal Catheter

- Catheter disconnection
- Catheter kinking
- Catheter fracture
- Catheter migration (unrelated to surgical complication)
- Cerebrospinal fluid (CSF) leak
- Disconnection
- Erosion
- Fibrosis
- Infection in intrathecal space, including meningitis
- Inflammatory mass formation (e.g., granuloma)
- Malpositioning
- Nerve damage
- Pain on injection
- Poor radiopacity
- Post dural puncture headache
- Reaction to catheter materials
- Reversible or irreversible partial or complete occlusions

- Spinal cord pressure leading to paralysis
- Spinal cord trauma, perforation, laceration
- Subcutaneous catheter tract infection
- Subcutaneous tunnel infection
- Tears/breaks

IX. SUMMARY OF PRECLINICAL STUDIES

Verification Activities
Product and component verification testing was completed to demonstrate that the finished device performs in accordance with design specifications. A comprehensive list of verification activities is contained in the Design Verification Matrixes. The section below provides an overview of these verification activities.

Pump Qualification
Flow accuracy of the pump at constant flow, multiple rate and demand bolus programs demonstrated performance that met product flow accuracy specifications. Flow testing at temperature (35-40°C), pressure ranges (10.1 – 16.7 psig) and reservoir fill levels characterized the affects on performance. These affects are shown in FIGURES 4-6.

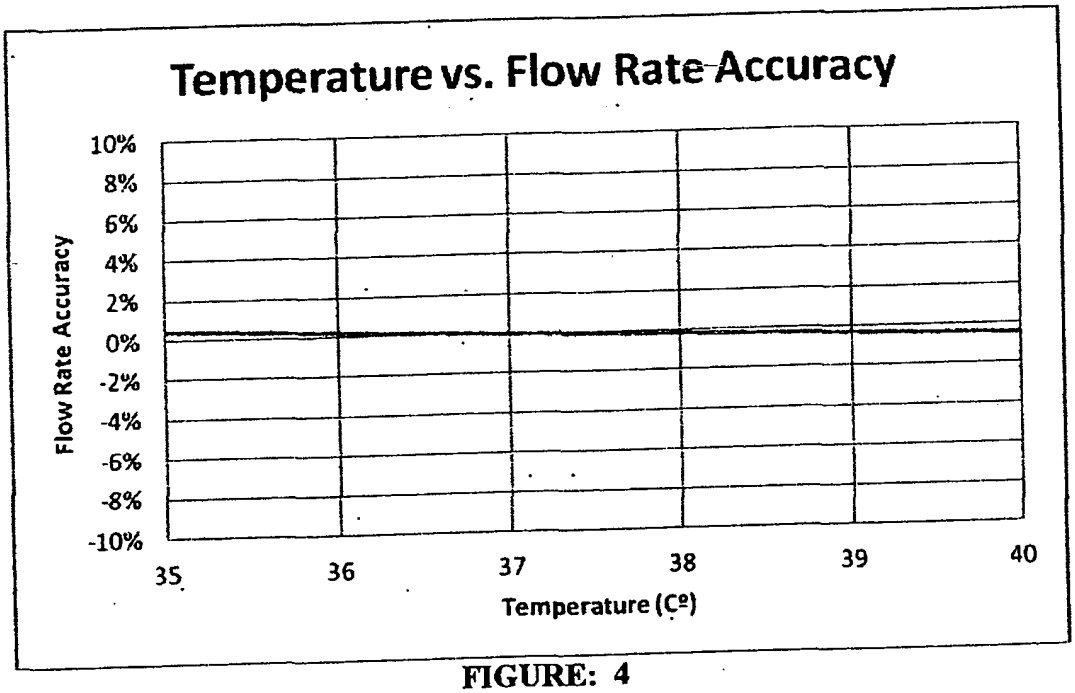


FIGURE: 4

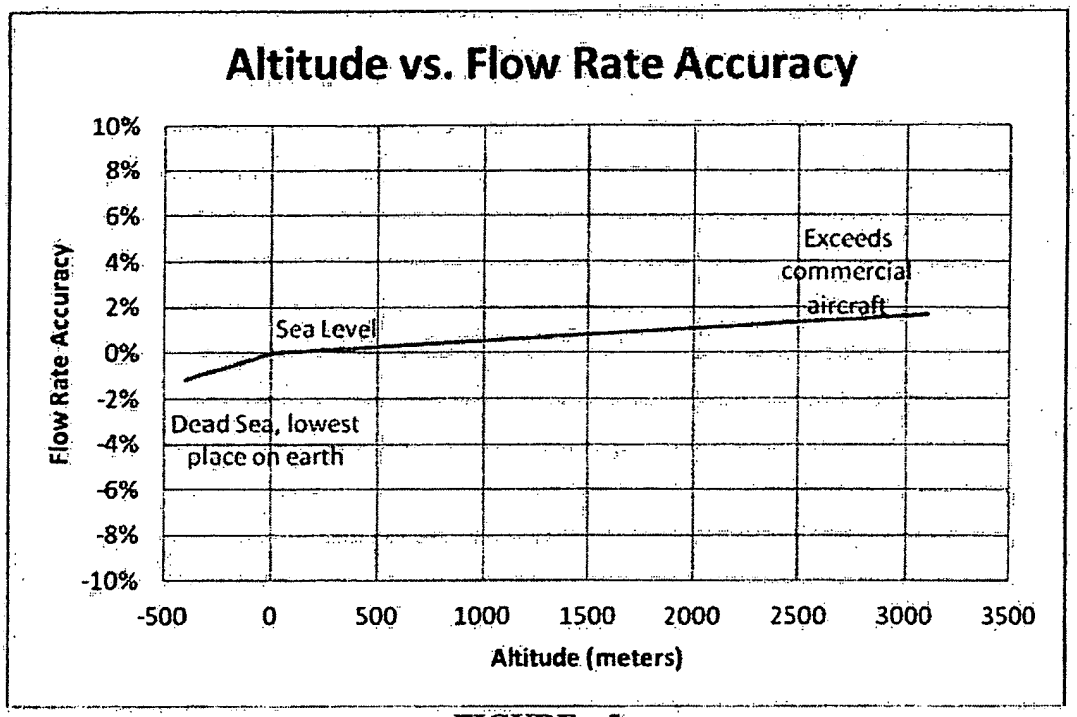


FIGURE: 5

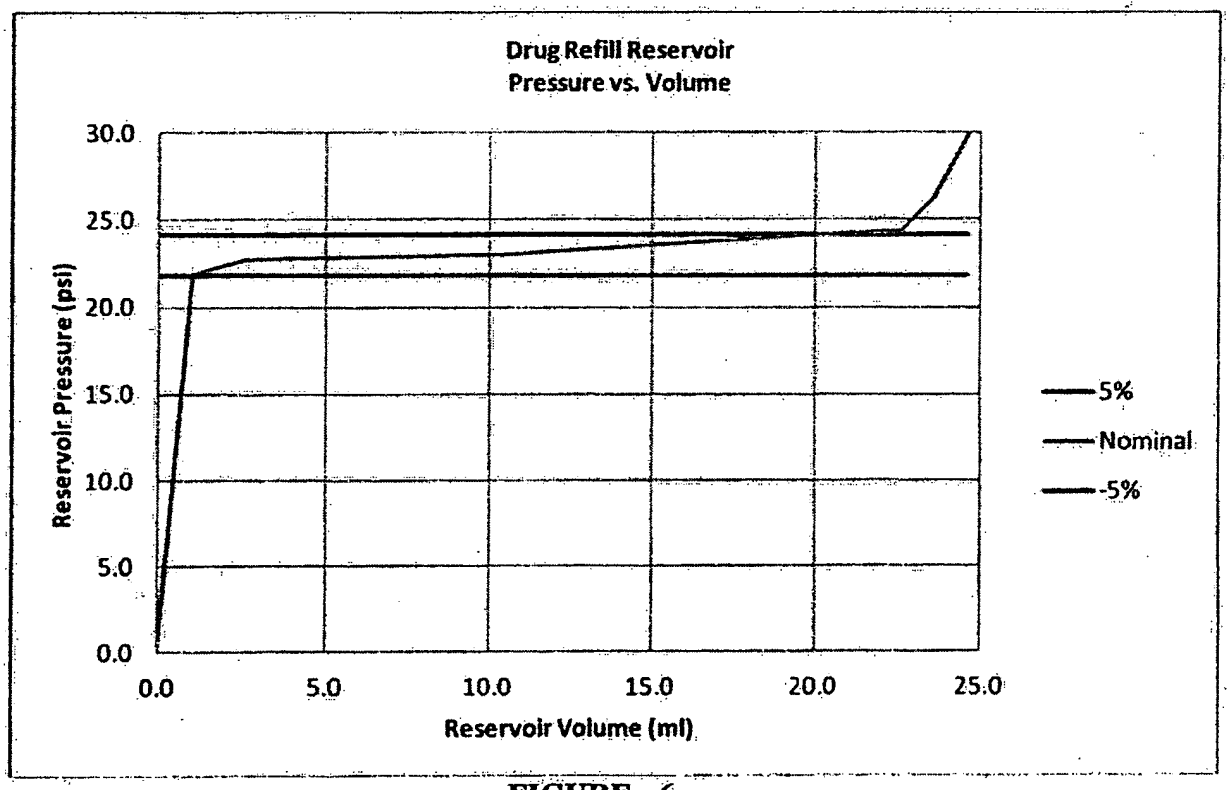


FIGURE: 6

Qualifications included life testing of the drug metering system and pump battery. The results of these evaluations are shown in FIGURE 7.

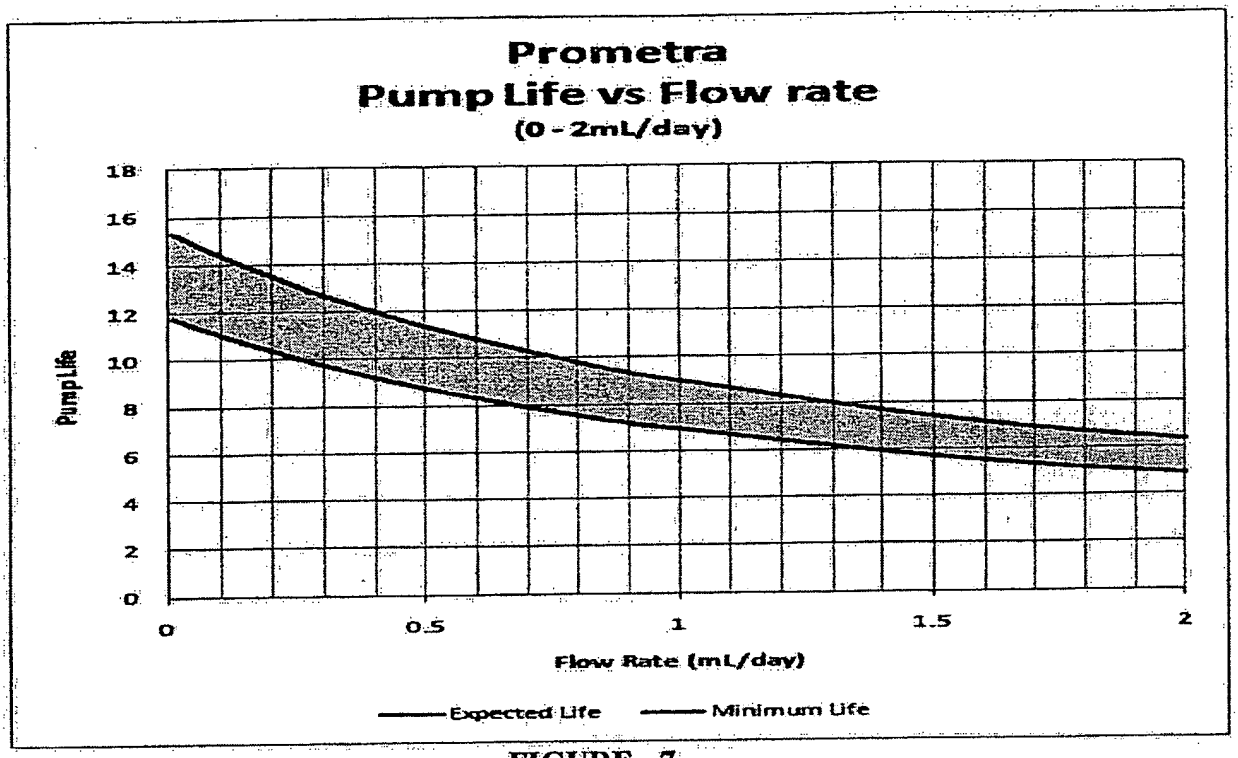


FIGURE: 7

Component Qualifications
Qualification testing verified performance of the components within pumps, including the bellows, refill, and catheter access port (CAP) septums. Average septum puncture life was demonstrated at greater than 1000 punctures for both the Refill and CAP.

Catheter testing included assessment of mechanical and functional characteristics, in addition to the connection integrity with pump system. Connection strengths of > 1.1lb were demonstrated between the catheter and pump connection.

Drug Compatibility and Stability
In-vitro Drug stability and compatibility testing performed on the pump indicates that Infumorph is stable for 90 days.

In-vitro stability was evaluated with the pump/catheter operating at 37°C over subsequent refill periods. The pump and catheter were evaluated regarding flow performance and stability of Infumorph.

The study observed acceptable results for assay, degradation products, impurities, leachables and extractables.

When first filled, the Prometra Pump has a small amount (2-3ml) of sterile water in the pump. As a result, there is an approximate 13% dilution of morphine sulfate in the initial filling of the 20mL drug reservoir.

Electrical Safety
Electrical engineering review of electronic components, including battery, valve, programmer, and electronic assemblies, demonstrated that electrical safety was adequately demonstrated through the life of the device.

17

Data demonstrated compliance with electrical safety standard, IEC 60601-1, 2nd edition.

Electromagnetic Compatibility
The Prometra Programmable Pump System contains two devices that include Electronics and Software; the Prometra Programmable Implantable Pump and Programmer. The programmer communicates with the pump through magnetic induction, which transmits drug delivery instructions from the programmer to the pump and delivery information from the pump to the programmer. All communication functions are initiated and controlled through the programmer.

The Prometra Programmable Pump and Programmer communication is performed by magnetic inductance through near field magnetic induction pulses. This communication is wireless in that it utilizes electromechanical waves rather than wire conductors for its communication linkage. This Pump/programmer telemetry is accomplished by the transmission of a series of magnetic pulses to and from the pump.

It was demonstrated that the device meets the following standards:

- IEC 60601-1 (Medical electrical equipment - Part I: General requirements for safety),
- IEC 60601-1-2:2001 (Electromagnetic emissions and immunity requirements for medical electrical equipment – Group 1 Equipment, Class B for non-life supporting equipment).

The pump and programmer were tested for radiated emissions, conducted emissions, radiated radio-frequency immunity, electrical fast transient immunity, electrostatic discharge immunity, surge immunity, conducted radio frequency immunity, magnetic field immunity, voltage dips and interrupts immunity, and harmonic emissions and voltage fluctuations/flicker tests.

Magnetic Resonance Imaging (MRI) Compatibility
FDA reviewed testing performed to demonstrate the effects of a static magnetic field, pulsed gradient magnetic fields, and radiofrequency pulses on the device, as well as MRI image artifacts caused by the device.

Testing was performed at 1.5 Tesla magnetic field.

Based on the heating study, a temperature increase of 2°C was observed after 15 minutes of RF application. Without the pump in place the temperature increase was 1°C. The Specific Absorption rate (SAR) for this application was about 1.5 W/Kg.

Based on the study report, the pump was found to have a significant magnetic deflection effect and also caused severe image artifacts. The pump deflected by 88°. Accordingly, this device did not pass the ASTM criteria of 45°. The qualitative torque measured was +4 (very strong torque) and is considered a significant risk in the MRI environment.

A signal void is caused by the device approximately 400 to 600 cm^2.

The device is MR Unsafe.

See the warnings in the physician and patient instructions for use regarding necessary steps that must be taken should an MRI be needed for a patient implanted with the Prometra® Programmable Infusion Pump System.

Computed Tomography (CT) Compatibility
The implanted pump and catheter system were evaluated for compatibility with CT scans. The pump samples under test were programmed to a flow rate of 28mL/day, and implanted into a torso model. The catheter tip was placed in the spinal segment T11-T12 of the model.

The CT scan focused on a 4-5inch length around the catheter tip. Scan settings are summarized in Table 2 below.

Table 2.– CT Scan Settings

Scanner	Toshiba – Aquillon 64		
Pump Sample	#1	#2	#3
Scan Mode	Helical	Helical	Helical
Total mAs in Study	5092	1329	1324
Total Scan Time (s)	82.36	17.86	17.86
Total DLP (mGy-cm)	50.5	275.9	271.7

Biocompatibility
The implanted pump system consists of a subcutaneously implanted pump and implanted intrathecal catheter, and is categorized as a permanent implant in contact with tissue/bone.

The components of the device in direct and indirect contact with the tissues are discussed below.

Direct tissue contact components:
Pump - titanium, silicone elastomers, polyphenylsulfone, and silicone adhesive.
Catheter - silicone elastomers, barium sulfate, tungsten, polyacetyl resin, ink and stainless steel.

Indirect tissue (fluid pathway) components:
Pump - titanium, silicone elastomers, polyvinylidene fluoride, polyphenylsulfone, MP35N metal (nickel-cobalt-chromium-molybedenum alloy), stainless steel (AL29-4, 316L).
Catheter - silicone elastomers, stainless steel, hydroglide hydro gel coating and plastic needle hubs (polypropylene and acrylic based).

As part of preclinical testing of the Prometra™ Programmable Infusion Pump System, biocompatibility studies were conducted to ensure that the components and the finished device are safe and perform in accordance with the design specifications.
Biocompatibility testing was performed following the International Organization for standardization (ISO) guidelines ISO 10993, "Biological Evaluation of Medical

Devices," and the guidance document released in 1995 by the U.S. FDA Blue Book Memorandum #G95-1, entitled "Use of International Standard ISO-10993, 'Biological Evaluation of Medical Devices'--Part-I: Evaluation and Testing."

The materials that make direct contact with tissue/bone and the indirect contacting materials were evaluated. The ISO 10993 Standard and the U.S. FDA Blue Book Memorandum #G95-1 were used as guidance in determining the appropriate tests for the device.

Tables 3 and 4 lists the tests conducted and the results for biocompatibility testing of the pump and intrathecal catheter, respectively.

Table 3 – Biocompatibility Test Results for the Pump

TEST	Results
L929 MEM Elution Test ISO 10993-5	Pass
Skin Sensitization Kligman Maxi. ISO 10993-10	Pass
Reverse Mutation Assay - S. typhimurium and E. coli ISO 10993-3	Pass
Chromosomal Aberration Assay ISO 10993-3	Pass
Rodent Bone Marrow Micronucleus Assay (38 animals) ISO 10993-3	Pass
Intracutaneous Injection ISO 10993-10	Pass
Systemic Injection IS010993-11	Pass
Rabbit Pyrogen (Material Mediated) IS010993-11	Pass

Table 4 – Biocompatibility Test Results for the Intrathecal Catheter

TEST	Results
L929 MEM Elution Test ISO 10993-5	Pass
Skin Sensitization Kligman Maxi. ISO 10993-10	Pass
Reverse Mutation Assay- S. typhimurium and E. coli ISO10993-3	Pass
Chromosomal Aberration Assay IS010993-3	Pass
Rodent Bone Marrow Micronucleus Assay (38 animals) ISO 10993-3	Pass
Intracutaneous Injection ISO 10993-10	Pass
Systemic Injection ISO 10993-11	Pass
13 Week Intramuscular Implantation ISO 10993-6	Pass

Long term Intramuscular Implantation (26 weeks) ISO 10993-6	Pass
Rabbit Pyrogen (Material Mediated) ISO 10993-11	Pass

Package and Sterilization Qualifications
Qualification testing of the pump and accessories; catheter, tunneler, Refill Kit and CAP kit packaging, consisted of environmental stress conditioning including temperature & humidity conditions, vibration, and drop testing. Environment exposure testing confirmed the pump remains functional after temperature, vibration, and shock exposures are applied to the pump. These evaluations demonstrated packaging is acceptable to simulated shipping and transit conditions.

Validation of the pump sterilization (Moist Heat) and accessories sterilization (ethylene oxide gas) demonstrates that the sterilization processes achieve a sterility assurance level of 10^{-6}.

Expiration dating for this device has been established and approved for each separately packaged component of the Prometra Programmable Infusion System as follows:

- Prometra Pump: 2 years
- Intrathecal Catheter Kit: 2.75 years
- Catheter Access Port Kit: 4.91 years
- Pump Refill Kit: 4.91 years
- Tunneler Kit: 4.91 years

Software Verification and Validation
Software documentation has been provided as recommended the May 2005, FDA Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices.

FDA has reviewed the following software documents:

Table 5 – Software Documentation

Level of Concern: Major	
	Acceptable
Software description:	Yes
Device Hazard Analysis:	Yes
Software Requirements Specifications:	Yes
Architecture Design Chart:	Yes
Design Specifications:	Yes
Traceability Analysis/Matrix:	Yes
Development:	Yes
Verification & Validation Testing:	Yes
Revision level history:	Yes
Unresolved anomalies:	Yes

Animal Studies

1. Trial A (Sheep Study)

Design
The first groups of animal studies were designed to address multiple objectives, including:

- Qualitatively evaluate the ease of implantation regarding the size/shape of the pump, suture anchors, and connection to catheter, catheter implantation, tunneling, and fixation of catheter.
- Qualitatively evaluate the instructions for use regarding surgical implantation of the pump and catheter and the use of the accessories during the implantation process.
- Qualitatively evaluate the refill and bolus kit procedures related to the ease of use of the device and adequate instructions for use regarding these procedures and kits.
- Evaluate the pump flow rate accuracy as measured clinically;
- Qualitatively evaluate the ease of use of the programmer;
- Record conventional post-implant histological assessment of the tissue response to the implanted product

Methods
A total of three (3) sheep were implanted with the Prometra Pump Systems. All sheep received a continuous intrathecal infusion of 0.9% Sodium Chloride for Injection, USP (preservative – free) for 12 weeks. Clinical observations were performed daily and refill tests once every 28 days. All sheep were euthanized between 12-13 weeks post implantation.

Results
- Results did not identify problems with the refill and bolus kit procedures. Final human factors validation studies were used to determine that use safety risks were mitigated.
- The flow rates for each infusion period for a given animal were fairly consistent from period to period with no more than a 12 percent difference between the calculated flow rates (maximum and minimum values).
- Results did not identify programming difficulty. Final human factors validation studies were used to determine that use safety risks were mitigated.
- The pump in each animal was surrounded by thickened tissue that corresponded to fibrosis microscopically (device encapsulation).
- Study design was not a controlled toxicology study and did not characterize local tissue reactions.

2. Trial B (28 Day Sheep Intrathecal Toxicology Study)

Design
This study was designed to provide a detailed neuro-toxicological assessment of the Prometra Pump and catheter system to definitively characterize the local tissue reaction in the intrathecal space compared to the Medtronic Synchromed II Pump and catheter

system. Medasys developed a research protocol to evaluate the equivalency of the Medasys and Medtronic catheters, including any potential neuro-toxicological effects.

Endpoint
The similarity in overall design and construction between the Medasys and Medtronic designs should not have dissimilar neuro-toxicological results.

Methods
Sixteen (16) sheep were used in this study, of which eight (8) were implanted with the Medasys Prometra Pump and catheter and eight (8) were implanted with the Medtronic SynchroMed II Pump and catheter. Within the Medasys study group, four (4) sheep were infused with sterile saline (as a control) and four (4) sheep were infused with morphine sulfate (Infumorph 200, Baxter Healthcare) at a programmed daily dose of approximately 6 mg/day. The same control and morphine sulfate infusion scheme was used with the Medtronic sheep study group.

Results
The gross and microscopic changes in animals treated intrathecally with either saline or morphine using the Prometra system was similar to those produced by the Synchromed II system.

Human Factors
Simulated Use Testing was performed to validate that the intended design of the Prometra System meets the needs of the user. The testing involved a review of the instructions for use (IFU), the programmer technical manual, the implantation of the pump and catheter, programming the pump for various operations, as well as accessing the pump once implanted.

The final validation study included seventeen (17) representative users. Users interacted with the programmer within use scenarios that required performance of all essential tasks. The human factors study was designed in accordance the FDA's Human Factors guidance: Medical Device Use Safety: Incorporating Human Factors in the Risk Management

X. SUMMARY OF PRIMARY CLINICAL STUDY

Medasys, Inc. performed a clinical study with Prometra® Programmable Infusion Pump System for continuous intrathecal infusion of Infumorph in the US under IDE # G060192. A summary of the clinical study is presented below.

A. Study Design

Patients were treated between March 10, 2007 and February 25, 2008. The database for this PMA reflected data collected through March 3, 2008 and included 110 patients. There were seven (7) investigational sites.

This study was an uncontrolled, non-randomized, open-label, one arm, multi-center study of the Prometra® Programmable Infusion Pump System. Standard statistical methods were employed to analyze all data. Assumptions of normality were tested

with the Shapiro-Wilks test. If the distributional assumptions were violated, nonparametric techniques such as Wilcoxon's Signed-Rank test were employed.

Primary Objectives

- To demonstrate that the Prometra® Programmable Infusion Pump System accurately and safely delivers Infumorph into the intrathecal space, as programmed.

Secondary Objectives

- Evaluation of the safety profile of the Prometra® Programmable Implantable Pump System, as determined by the rate of device-related serious adverse events and device complications through six-months post-implantation

- Evaluation of the degree of pain relief achieved with chronic intrathecal infusion of Infumorph delivered via the Prometra Programmable Implantable Pump System.

The primary endpoint will be considered to be met if the 90% confidence limits on the delivered to programmed drug volume (DP) ratio are within the 85% to 115% range.

Statistically significant reductions in pain are not required for this trial to be considered a success.

1. Clinical Inclusion and Exclusion Criteria

Enrollment in the pivotal study was limited to patients who met the following inclusion criteria

1. Patient was to have been suffering from cancer pain requiring strong opioids OR has chronic, non-malignant pain with an average daily pain score of 4/10 or greater on a scale of 0 to 10 OR Patient was to need an implantable pump system (pump & catheter) replaced due to malfunction or battery depletion. Patient must have had a documented history of sufficient pain relief with intrathecal morphine sulfate infusion.
2. Patient was to have been 18 years of age or older.
3. Patient was to have a life expectancy of > 6 months.
4. Patient was to have a documented failure to respond to less invasive methods of pain control, including attempts to eliminate physical and behavioral abnormalities that may cause an exaggerated reaction to pain.
5. Patient was to have pain ineffectively controlled by single or multiple systemic (oral, rectal, transdermal or intravenous) analgesic treatments or patient experienced intolerable side effects from such treatment.
6. Patient was to have had a successful trial of morphine sulfate (intrathecal or epidural) for relief of the target symptoms.
7. Patient was to have agreed to obtain narcotic prescriptions only from the investigator.
8. Patient was to provide written informed consent to participate in the study.
9. Patient was to have been considered by the investigator to be a medically and psychologically appropriate candidate for pump implantation.

24

10. Investigator and/or study coordinator was to have considered the patient to be able and willing to fulfill all study requirements.

Patients were <u>not</u> permitted to enroll in the pivotal study if they met any of the following exclusion criteria:

1. Patient was to have had existing damage to the spinal column observed via magnetic resonance imaging (MRI) of spine that, in the opinion of the Investigator, would prevent intraspinal drug administration (e.g. cord compression from metastatic tumor that could obstruct catheter placement or drug flow). If the patient had a medical condition that contraindicates MRI, the investigator was to have proceeded with the closest appropriate study (i.e. CT scan, X-ray) to rule out any spinal abnormalities that would prevent intraspinal drug administration.
2. Patient was to have a systemic infection.
3. Patient's anatomy was not large enough to accommodate the pump's size and weight.
4. Patient was pregnant or breast-feeding or was of child-bearing potential and not employing effective birth control.
5. Patient had known allergies or sensitivities to pump system materials (e.g., silicone rubber, titanium, polyphenylsulfone, acetal resin, polyvinylidene fluoride, tungsten).
6. Patient had known allergies to morphine or would be contraindicated for morphine, based on the drug labeling.
7. Patient had a major coexisting medical condition (such as gastrointestinal problems, respiratory reserve / lung function problems, or heart conditions that cannot tolerate further lowering of blood pressure) that, in the opinion of the investigator, contraindicates an implantable pump.
8. The patient was to require MRI evaluation post-implantation.
9. Patient had other implanted cardiac electronic devices.
10. Patient had an occupation where he/she would be exposed to high current industrial equipment, powerful magnets or transmitting towers, such as, electricians, electrical engineers or MRI technicians.
11. Patient was unable to participate in all necessary study activities due to physical or mental limitations.
12. Patient was unable or unwilling to return for all required follow-up visits.
13. Patient was unable or unwilling to sign the informed consent document.

2. <u>Follow-up Schedule</u>

Patients attended a post-operative follow-up visit approximately 10 days after implantation for assessment of wound healing. After completion of the postoperative visit, patients attended visits on a monthly basis at 1, 2, 3, 4, 5, and 6 months post-implantation. During each monthly follow-up visit, the study device was refilled and infused volumes of medication were documented. Patients requiring additional visits (for refill/reprogramming of the study device or care for adverse events) before the next scheduled monthly visit attended unscheduled visits, as needed.

After completion of the Month 6 visit, patients entered the Long-Term Phase of the study and attended follow-up visits on a quarterly (every 3 months) basis until the study device was explanted or becomes commercially available or the subject expired.

Table 6 – Follow up Schedule

Study Procedures	Screening[1]	Baseline	Acute Phase			Long Term Follow-Up	
		Day of Implantation	Day 10 (±5 days)	Months 1-6[2] (± 7 days)	Unscheduled Visits	Quarterly[3] (every 3 months) (± 30 days)	Unscheduled Visits
Provision of informed consent	X						
Review of entrance criteria	X						
Medical history	X						
Pain history	X						
Physical examination	X						
Neurological examination	X		X[4]	X[4]			
MRI of spine	X						
Serum β-HCG pregnancy test	X[5]						
Patient Questionnaires (NRS, VAS, ODI)	X	X		X	X		
Pump implantation		X					
Wound assessment			X				
Pump fill/refill		X		X	X[6]	X	X[7]
Spinal X-ray		X					
Documentation of concomitant medications[8]		X	X	X	X	X	X
Documentation of AEs		X	X	X	X	X[9]	X[9]
Documentation of DCs		X	X	X	X	X	X

[1] All screening assessments are to be completed within 60 days prior to implantation. MRI's (or similar procedures to evaluate the spine) will be accepted if completed within six months from the date of implantation.

[2] Monthly follow-up visits are to be conducted monthly from the day of implantation, +/- 7 days.

[3] Patients are to attend long-term follow-up visits for refills, which must be at least every three months (+/- 30 days) until the Prometra System is explanted, the subject expires, or the Prometra System is approved for commercial use by the FDA.

[4] If results differ from Screening results and are clinically significant, a computed tomography (CT) myelogram should be performed to further evaluate the change.

[5] Must be completed within 3 days prior to implantation. For female patients of childbearing potential only.

[6] Refill is only required if it has been more than 30 days since previous refill.

[7] Refill is only required if it has been more than 90 days since previous refill.

[8] During the Acute Phase record only pain and AE-related meds; during the Long-Term Phase record only pain, serious adverse event (SAE) related, and device related adverse event (DRAE) related meds.

[9] Only SAE's and DRAE's will be reported on the CRF during the long-term follow-up.

3. Clinical Endpoints

The primary endpoint of the study was:

The accuracy of the volume of medication delivered by the Prometra® Programmable Implantable Pump System relative to the volume programmed for delivery, as determined at the time of pump refill (i.e., delivered to programmed drug volume (DP) ratio). The primary endpoint will be considered to be met if the 90% confidence limits on the DP ratio are within the 85% to 115% range.

B. Accountability of PMA Cohort

At the time of database lock, of 110 patients enrolled in PMA study, 58% (64) patients completed the 6 month visit surpassing the minimum required for primary endpoint analysis and completion of the study. Patient accountability at each scheduled visit is detailed in Table 7.

Table 7 - Patient Accountability

Status	*Patient Accountability (Number of enrolled = 110) Month 1 N(%)*	*Month 2 N(%)*	*Month 3 N(%)*	*Month 4 N(%)*	*Month 5 N(%)*	*Month 6 N(%)*	*Month 9 N(%)*
Discontinued							
Death	-	-	-	*1 (1)*	*1(1)*	-	-
Adverse Event	*2 (2)*	*3 (3)*	*3(3)*	-	-	*1(1)*	*1 (1)*
Patient Withdrew Consent	-	-	*1(1)*	-	-	*1(1)*	-
Not Eligible for Interval (previously discontinued)	*N/A*	*2(2)*	*5(5)*	*9(8)*	*10(9)*	*11(10)*	*13(12)*
Unavailable for Visit:							
Missed Visit	-	*1(1)*	*1(1)*	-	*1(1)*	-	-
Lost to Follow-up	-	-	-	-	-	-	-
Available for Analysis	*108 (98)*	*103 (94)*	*95 (86)*	*87 (79)*	*72 (65)*	*64 (58)*	*21 (19)*
% Accountability= visits completed/(110-discont.-not eligible)	*100%*	*98%*	*94%*	*87%*	*73%*	*66%*	*22%*

C. Study Population Demographics and Baseline Parameters

Table 8 - Study Demographics

Demographic	ITT and MITT Populations (N=110)	PP-PA Population (N=107)	PP-PR Population N=102)
Gender - N (%)			
Male	59 (54%)	56 (52%)	54 (54%)
Female	51 (46%)	51 (48%)	47 (46%)
Age - (years)			
N	110	107	102
Mean	55.6	55.7	54.8
SD	13.3	13.3	13.0
Median	54.6	54.6	53.9
Range	28-84	28-84	28-83
Race – N (%)			
White	104 (95)	101 (94)	96 (94)
Black or African American	5 (5)	5 (5)	5 (5)
Hispanic	1 (1)	1 (1)	1 (1)

Table 9 - Pain History

Variable	ITT and MITT Populations (N=110)
Duration of Pain (N ± SD)	12.4 ± 10.0 years
Pain Category – N (%)	
Neuropathic	64 (58)
Nociceptive	12 (11)
Both	34 (31)
Causes of Pain[1] - N (%)	
Chronic Regional Pain Syndrome	24(22)
Vertebral Body Compression Fractures	6 (6)
Post Lumbar Spine Surgery with Pain	60 (55)
Post Cervical Spine Surgery with Pain	14 (13)
Phantom Limb Pain	0
Post Thoracotomy Pain Syndrome	3 (3)
Arachnoiditis	26 (24)
Intractable Back Pain	57 (52)
Cancer Pain	3 (3)
Other	70 (64)

Variable	ITT and MITT Populations (N=110)
Type of Pain[1] - N (%)	
Aching	90 (82)
Burning	74 (67)
Pins and Needles	54 (49)
Sharpness	79 (72)
Numbness	62 (56)
Cramping	42 (38)
Other	52 (47)
Area of Pain Involvement - N (%)	
Generalized	12 (11)
Localized[1]	98 (89)
Head	16 (16)
Arms/Hands	26 (27)
Hips	44 (45)
Legs/Feet	75 (77)
Chest	8 (8)
Shoulder	26 (27)
Back	78 (80)
Neck	31 (32)
Other	20 (20)

[1] Percentages may add up to greater than 100% because patients may be counted in more than one category.

D. Safety and Effectiveness Results

The primary endpoint has been met. The 90% confidence interval of the DP Ratio (95.9 – 97.7%) is well within the required range (85 - 115%).

Table 10 - Accuracy Results

Per Patient DP Ratio	ITT Population (N=110)	MITT Population (N=110)	PP-PA Population (N=107)
N	107[1]	107[1]	107
Mean	96.7	96.7	96.8
SD	5.6	5.8	5.5
Median	97.0	97.0	97.0
Range	71.9 – 127.1	71.9 – 127.1	81.8 – 127.1
90% confidence interval of mean	95.8 – 97.6	95.7 – 97.6	95.9 – 97.7

[1] Three patients had their pump explanted prior to having a refill.

Adverse effects that occurred in the PMA clinical study:

Table 11 - Summary of All Adverse Events (AE)

Category	ITT Population (N=110) N (%)
Patients with at least one AE	107 (97)
Patients with at least one SAE	27 (25)
Patients with at least one DRSAE	3 (3)
Patients discontinued due to AEs	9 (8)

Table 12 - Adverse Events Reported as Possibly, Probably, or Definitely Related to the Device or Study Procedure

System Organ Class	Preferred Term	ITT Population (N=110) N (%)
Ear and Labyrinth Disorders	Tinnitus	1 (1)
Gastrointestinal Disorders	Nausea	15 (14)
	Vomiting	8 (7)
	Abdominal Pain	1 (1)
	Constipation	1 (1)
	Oral Mucosal Blistering	1 (1)
General Disorders and Administration Site Conditions	Implant Site Pain	20 (18)
	Implant Site edema	11 (10)
	Implant Site Erythema	9 (8)
	Implant Site Swelling	4 (4)
	Pain	4 (4)
	Implant Site Inflammation	3 (3)
	Drug Withdrawal Syndrome	2 (2)
	Implant Site Haemorrhage	2 (2)
	Pyrexia	2 (2)
	Tenderness	2 (2)
	Catheter Site edema	1 (1)
	Implant Site Bruising	1 (1)
	Implant Site Effusion	1 (1)
	Implant Site Hypersensitivity	1 (1)
	Implant Site Irritation	1 (1)
	Implant Site Necrosis	1 (1)
	Edema Peripheral	1 (1)
Immune System Disorders	Hypersensitivity	1 (1)

System Organ Class	Preferred Term	ITT Population (N=110) N (%)
Infections and Infestations	Incision Site Infection	4 (4)
	Extradural Abscess	1 (1)
	Implant Site Cellulitis	1 (1)
	Spinal Infection Viral	1 (1)
Injury, Poisoning and Procedural Complications	Procedural Pain	37 (34)
	Post Lumbar Puncture Syndrome	9 (8)
	Wound Secretion	9 (8)
	Seroma	4 (4)
	Wound Dehiscence	3 (3)
(Injury, Poisoning and Procedural Complications, continued)	Excoriation	1 (1)
	Hip Fracture[1]	1 (1)
	Procedural Nausea	1 (1)
Musculoskeletal and Connective Tissue Disorders	Back Pain	2 (2)
	Pain in Extremity	2 (2)
Nervous System Disorders	Headache	8 (7)
	Dizziness	3 (3)
	Intracranial Hypotension	2 (2)
	Balance Disorder	1 (1)
	Burning Sensation	1 (1)
	Diplegia	1 (1)
	Hypoaesthesia	1 (1)
	Neuropathy Peripheral	1 (1)
	Tremor	1 (1)
Respiratory, Thoracic and Mediastinal Disorders	Dyspnoea	1 (1)
	Respiratory Depression	1 (1)
Skin and Subcutaneous Tissue Disorders	Dermatitis Contact	5 (5)
	Pruritus	2 (2)
	Scab	2 (2)
	Ecchymosis	1 (1)
	Rash	1 (1)
Surgical and Medical Procedures	Surgery[2]	10 (9)
Vascular Disorders	Haematoma	1 (1)

[1] Event occurred while patient was being treated with a drug other than Infumorph via Prometra System

[2] Surgery to replace or revise intrathecal catheter

31

XI. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

In accordance with the provisions of section 515(c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the General Hospital and Personal Use Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

The Prometra System achieved the clinical study primary endpoint by accurately delivering the volume of Infumorph programmed for delivery. The 90% confidence interval of the Delivered to Programmed Ratio (*95.9 – 97.7%*) was within the required range (85 – 115%).

Improvements in pain and related disabilities from baseline were reported at the end of each month during the first six (6) months post-implant. Markers for effectiveness were derived from measurement of Visual Analog Scale (VAS) and Numerical Rating Scale (NRS) pain scales, as well as scores from Oswestry Disability Index (ODI) questionnaires. Few patients completed the protocol without confounding concomitant treatments for pain. Therefore, secondary objectives were not achieved.

Interpretation of the patient safety database was confounded by intrathecal administration of drugs that were not approved for that route of administration, concurrent use of a spinal cord stimulator, and differences in adverse events reported between the applicant's summaries and the electronically reported line data. The study also did not include a control.

Despite these limitations, there was no apparent safety signal or other systematic pattern of device-related adverse event noted.

The study demonstrates that the pump is able to accurately deliver the volume of Infumorph that is programmed for delivery.

Preclinical studies demonstrate that device specific risks to health are identified and controlled.

The data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use.

XIII. CDRH DECISION

CDRH issued an approval order on February 7, 2012. The final conditions of approval cited in the approval order are described below.

1. An in-vitro, in-use stability study, over refills of the pump for the intended use period. The study will characterize the long-term profile of extractable/leachable and impurities/degradation products and will address any impairment of pump system function.

2. A prospective, non-randomized, open-label, multicenter study to evaluate the long-term safety of the Prometra® Programmable Pump System.

The applicant's manufacturing facility was inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820).

XIV. APPROVAL SPECIFICATION

Directions for use: See device labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the device labeling.

Post-approval Requirements and Restrictions: See approval order.

How do valve-gated implantable drug pumps differ from peristaltic pumps?

Valve-gated drug pumps are newly approved by the FDA for delivering Infumorph® intrathecally. What is a "valve-gated" drug pump? How does this differ from the peristaltic technology that pain management physicians are familiar with? This white paper will outline the differences between these technologies, illustrating the effects of valve gating on drug delivery, and how these changes may positively impact patient management.

Implantable Drug Pumps

Implanted devices are under significant engineering constraints. Weight, longevity, durability, and battery life are but a few of the constraints that limit engineers from utilizing the same components as external pumps. In order to achieve an optimal design, engineers are required to make trade-offs between the various capabilities for different components.

As an example of an engineering trade-off, it is helpful to review the "metal bellows" reservoir. This reservoir design is used in all implantable drug pumps, primarily because it is an energy-efficient design. The design consists of two chambers, one within the other. Fluid is stored in the inner chamber, which expands when filled. The outer chamber contains pressurized gas that forces on the inner chamber to contract. If allowed to, the inner chamber would automatically empty its drug in a response to the gas pressure (see Figure 1).

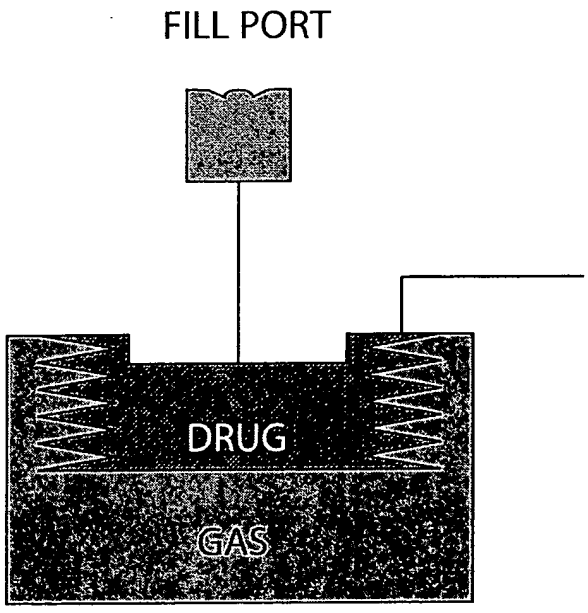


Figure 1: Metal Bellows Reservoir

As the inner chamber delivers fluid and the bellows contract, the pressure of the gas decreases, putting consistantly less pressure on the inner chamber to push drug into the rest of the pump. There may be significant pressure differences in the same pump on the day before and the day after a pump refill. The variation of force delivering drug as the reservoir empties may cause significant fluctuations in the amount of drug delivered to the dosing system (see Figure 2).

Gas pressure within the reservoir is also affected by alterations in the ambient pressure and temperature. Higher ambient pressure (at sea level) coupled with high temperatures and a full reservoir may lead to significantly higher pressure. For example, a patient with a full reservoir traveling from a low-altitude, high-temperature environment, such as Houston, to a high-altitude, low-temperature environment, such as Denver, may encounter problems. This could cause a decrease of as much as 24% in the amount of drug being delivered by the pump.[1]

Dosing fluctuations may impact therapy. Physicians may observe a resumption of symptoms around the time of refill. What physicians may not always observe is the cessation of symptoms once normal drug flow resumes. Thus, clinicians may consider a dose increase when none is warranted.

If delivering a drug with a narrow therapeutic window of safe, effective dosing, fluctuations caused by decreased reservoir pressure will be particularly noticeable. However, by making changes to the design of other components in the pump, such as the Dose Regulation System, these fluctuations and their effects on patient therapy can be minimized.

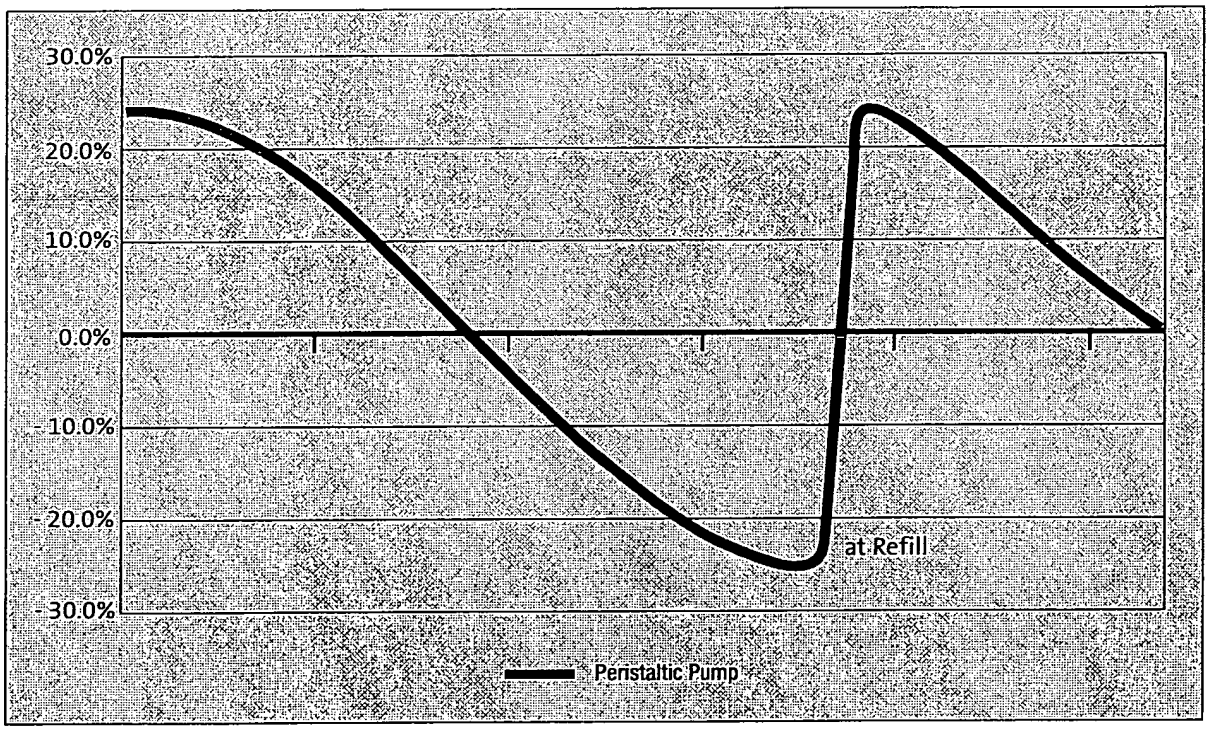


Figure 2: Pump Potential Dose Variation
(0.0% = Prescribed Dose)

Dose Regulation Systems

As described previously, fluid will leave the main reservoir immediately if it is not regulated. In programmable pumps, fluid is restricted from flowing freely out of the pump reservoir by the Dose Regulation System. The way this component functions is the principal difference between a peristaltic pump and valve-gated pump (see Figure 3).

The Dose Regulation System is the most mechanically complex component of an implantable pump and has a significant impact on several pump features. It affects:

- Reliability of dosing
- System-wide durability
- Device longevity

The Dose Regulation System can be likened to a throttle in an engine; it controls the speed at which the pump delivers medicine and the regularity at which it is delivered. Like a gas pedal, it has a major impact on the amount of energy used by the system. A more efficient Dose Regulation System may increase the battery life, use fewer moving components to help provide enhanced durability, and take into consideration fluctuations in the flow of fluid from the reservoir to improve the reliability of dosing.

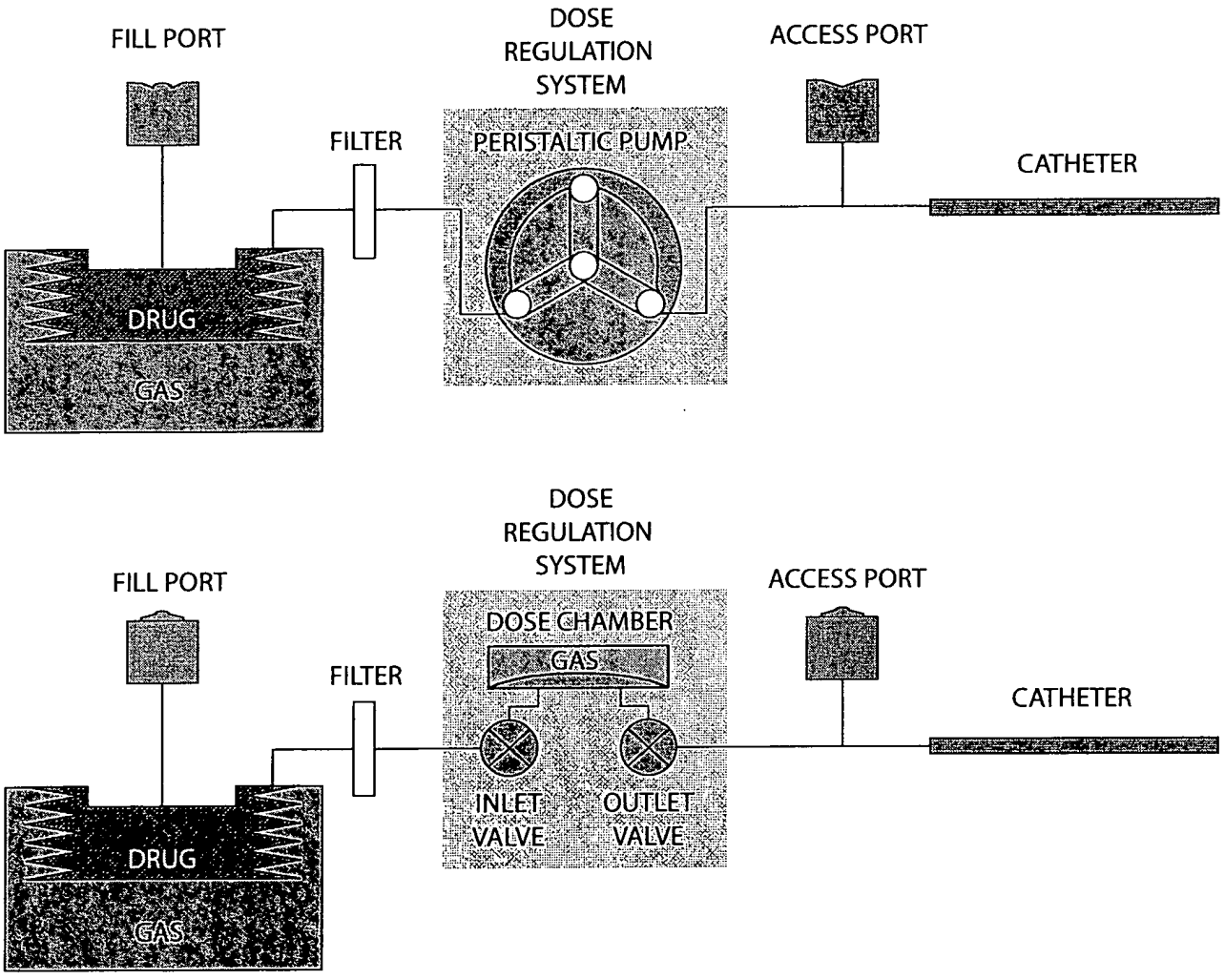


Figure 3: Flow Path Comparison Peristaltic vs. Valve-Gated Dose Regulation System

Peristaltic Pump Dose Regulation

The Dose Regulation System in a peristaltic pump consists of plastic tubing that runs from the reservoir to the catheter. This tubing is occluded by rollers at various points along the tubing path to control fluid flow. The rollers move over the tubing to force fluid to flow through the tubing at a specified rate. The rollers are connected to gears that are powered by a motor. There are several moving parts in this configuration. As with all mechanical devices, the more complex the device, the higher the likelihood that something may go wrong (see Figure 4).

Some systems are configured to always be in motion, in order to conserve battery power. Enhancing the battery life in this way, however, may have a deleterious effect on therapy, since this means the device can never be completely stopped. Even operating at the slowest speed, pumps can still deliver nearly 0.75 mL of fluid a day. The impact of this design feature is that if a patient requires a complete cessation of therapy, a complex series of steps must occur in which the drug is drained from the reservoir, the reservoir is filled with saline solution, and the catheter is aspirated. The pump cannot simply be stopped (see Figure 4).

Over time, continuing pressure by the rollers may change the pliability of the plastic tubing. As the pliability of the tubing changes, the amount of fluid that can be squeezed into the tubing by the pressure on the drug in the reservoir may also change. Essentially, each "dose" delivered by the rotation of the rotors changes as the tubing becomes more pliable, potentially affecting the overall accuracy of the system.

According to a study by DuPont engineers, "Available tubing for peristaltic pumps tends to shed particulates into the solution due to their poor abrasion characteristics."[2] Wear debris is produced because of repeated compression of the tubing as the rollers squeeze fluid via the peristaltic process. It is unclear what impact the creation and transmittal of plastic tubing wear debris may have on the patient in the long term.

From the above, it is clear that peristaltic pumps have several drawbacks:

- Complex nature of the gears and motor can affect the durability/longevity of the device
- Tubing pliability changes over time – affecting dose reliability
- Drugs may permeate the plastic tubing affecting the rollers, gears, and other components
- Rollers rubbing against and constricting the pliable tubing may wear the tubing

Valve-gated technology was developed in an attempt to minimize these potential effects, and to create an implantable pump that will have improved longevity, durability, and dose reliability.

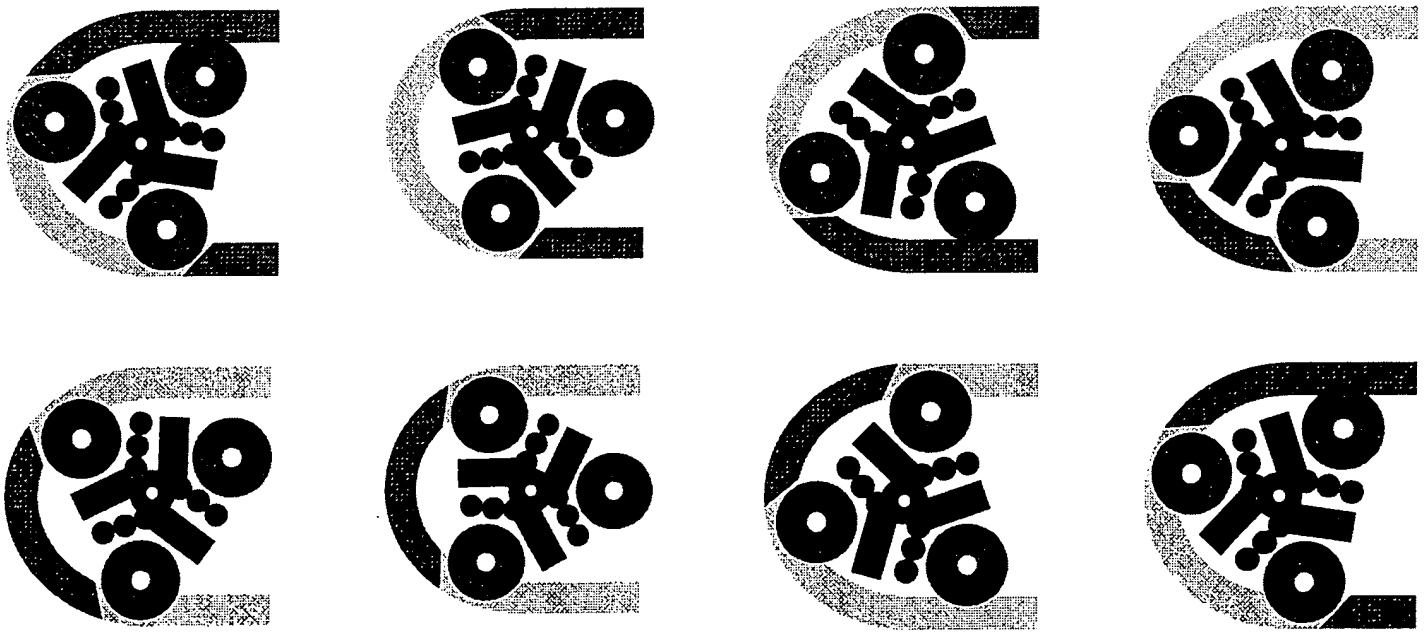


Figure 4: Peristaltic Pump Rollers Moving Drug Through Tubing

Valve-Gated Dose Regulation

In the Prometra® valve-gated pump, the Dose Regulation System consists of two valves and a Dosing Chamber, which together make up the Precision Dosing System.™ Fluid is regulated from streaming out of the reservoir by the first valve. This "inlet valve" allows fluid to flow into the Dosing Chamber. An "outlet valve" at the exit of the Dosing Chamber prevents fluid from flowing through the Dosing Chamber and into the catheter even when closed. Electronics control the flow of fluid by alternately opening the inlet and outlet valves, preventing both valves from opening at the same time. Drug enters and exits the Dose Regulation System when the valves are open (see Figure 5).

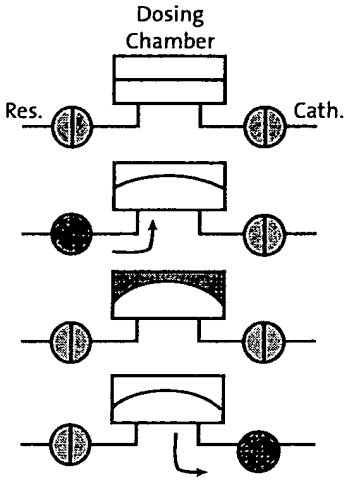


Figure 5: Dose Regulation System

The Dosing Chamber is engineered very much like the metal bellows reservoir – there is an inner, expandable chamber, and an outer, gas-filled chamber. The pressure of the dosing chamber is set to be much lower than the pressure of the reservoir, so that upon opening the inlet valve, fluid flows freely from the higher-pressure reservoir to the lower-pressure Dosing Chamber. The addition of a Dosing Chamber enables fluid to be measured, which may help prevent changes in reservoir pressure from impacting dose accuracy.

The reservoir gas pressure changes with environmental effects such as pressure, temperature, and reservoir level, just as it does with a peristaltic pump. In a valve-gated system, these fluctuations do not have a significant therapeutic effect on dose reliability (see Figure 6). This improvement in dose reliability can be attributed to the inclusion of a titanium Dosing Chamber for measuring doses, rather than using pliable tubing, as is done with peristaltic pumps. As a result, pressure, temperature, and changes in the reservoir level had minimal impact on dose reliability during clinical trials.[4]

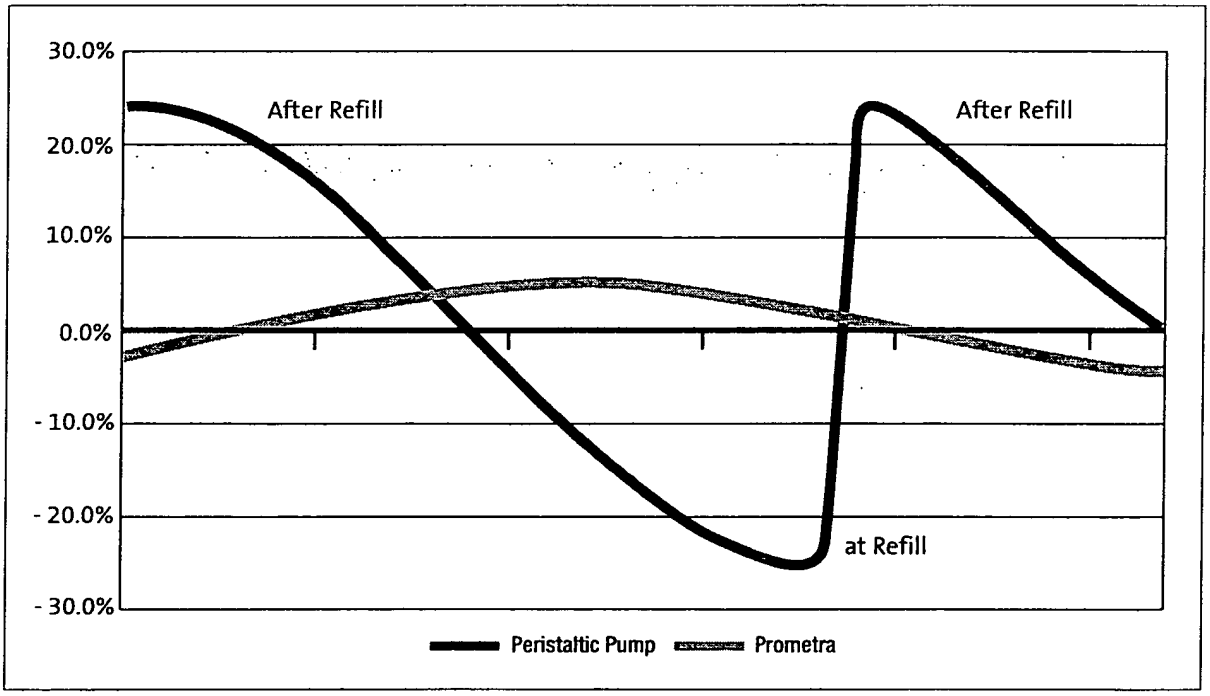


Figure 6: Potential Dose Variation (0.0% = Prescribed Dose)

In the valve-gated pump, the fluid pathway is 100% titanium, a biocompatible inert material which has been tested with Infumorph. Titanium does not interact with drugs nor can drugs permeate titanium to damage other components.

The only moving parts in the pump are the valves. By eliminating the motor, gears, and other moving parts, it is expected that the durability of the pump may significantly improve. Because the energy used by the microvalves is very low, the battery life may be longer (see Figure 7).

From the above it is clear that the valve-gated Dose Regulation System in an implantable pump may offer several advantages:

- Changes in reservoir gas pressure due to fluctuations in the refill level or environmental factors has minimal effect on dose accuracy
- Fluid pathway is enclosed in 100% titanium – not subject to permeability that has been experienced by peristaltic plastic tubing, causing corrosion and rotor stalls
- Fewer moving parts in valve-gated pumps (only the valves move) means less wear and tear and potentially better device durability
- More efficient overall design for valve-gated pumps results in longer battery life than currently available peristaltic pumps,[3] and thus potentially fewer replacement surgeries

Effects on Therapy

Choosing valve-gated over peristaltic pumps may have several potential advantages for patients. These advantages may include:

- Longer time between pump replacement procedures
- Better control over drug delivery
- Less dosing variability just before/after refills
- Less dosing variability if patient travels to higher/lower altitudes
- Less dosing variability if patient uses a spa or hot tub

Summary

There are several drawbacks to peristaltic technology in an implantable pump. Drugs flow through plastic tubes which are repeatedly constricted by rollers, causing potential wear and pliability changes over time. These alterations, along with succeptibility of the system to environmental factors such as ambient pressure, temperature, or level of fluid remaining in the reservoir may cause the pump to be less reliable than alternatives, potentially affecting patient management.

The rollers in peristaltic pumps are moved with a motor and gears. The plastic tubes in contact with the rollers have been known to be permeable – causing corrosion of the pump workings. Utilizing newer technology could potentially improve durability and battery life.

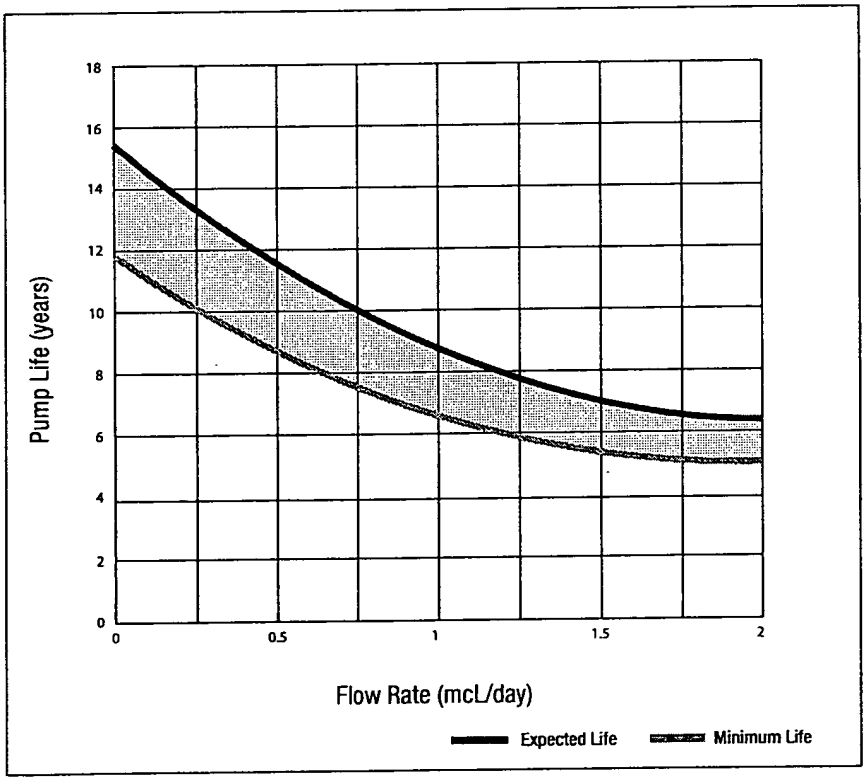


Figure 7: Battery Longevity

The valve-gated pump is designed to improve upon peristaltic technology by elimination the motor, gears, and rollers. They are replaced with a 100% titanium fluid pathway which includes a Dosing Chamber and microvalves to regulate drug flow. These features are designed to:

- Improve dose accuracy over the refill cycle
- Improve dose accuracy over the pump life
- Improve overall durability
- Improve battery life

Improved dose reliability might lead to less alterations in patient therapy as their reservoir empties, or as they experience changes in environmental conditions or weather that may alter the drug flow in peristaltic pumps. This could potentially prevent increases in dosing, possibly altering tolerance effects.

Similarly, improved durability and battery life could result in longer periods of time between pump replacement procedures, which could significantly benefit the patient's quality of life. The combination of benefits that valve-gated technology offers physicians could have a significant impact on improving patient therapy.

References

[1] Medtronic Instructions for Use, SynchroMed II

[2] Bahal SM, Romansky JM. Spalling and sorption of tubing for peristalitc pumps. Pharm Dev Tech. 2002; 7(3):317-323.

[3] Deer T, Rosen S, Dunbar E, Barsa J, Padda G, Dwarakanath G, Rauck R. Accuracy and effectiveness of morphine sulfate infusion via the Prometra programmable intrathecal infusion pump. Napa Pain Conference 2009. Napa, California.

Rx Federal Law (USA) restricts this device to sale by or on the order of a physician.

Unless otherwise indicated, ™ denotes a trademark, and ® denotes a registered trademark, of Flowonix Medical Inc. or their respective owners.

Flowonix™

Implanting Confidence®

Flowonix Medical Inc.
500 International Drive, Suite 200
Mount Olive, New Jersey 07828
973.426.9229 · 973.426.0035 (fax)
www.flowonix.com

PL-05030

Prometra Programmable Pump

A. Principles of Operation

The Prometra Programmable Flow Pump contains a titanium bellows drug reservoir. The reservoir propellant is stored within the rigid titanium housing surrounding the bellows drug reservoir and provides the driving pressure for pump. The driving pressure on the bellows reservoir forces drug through an outlet filter (0.22 microns), and into an electronically controlled flow metering subsystem composed of an inlet valve, accumulator, and outlet valve. The electronics are designed so that only one valve may be opened at any given time. When the inlet valve is momentarily opened, the accumulator is filled with approximately 2 microliters (ul) of additional drug by the accumulator diaphragm deflection. The accumulator diaphragm is pressurized on the non-drug side by a gas pressure that is lower than the bellows drug reservoir pressure. When the outlet valve is momentarily opened, the approximately 2 ul of drug stored in the deflected accumulator diaphragm is delivered past the catheter access port into the catheter for delivery to the intrathecal space. The delivered pump flow rate is controlled by the electronically programmed time intervals between the consecutive 2 ul delivered boluses.

B. Pump System Description

Pump Model	Prometra
External Properties	
Material	Titanium pump with white polyphenylsulfone access port
Thickness (including septum)	20 mm
Diameter	71 mm
Weight (empty)	150 g
Drug Reservoir	
Material	Titanium
Usable capacity	20 ml
Maximum usable capacity	23 ml
Reservoir pressure	Approx. 16.9 x 10^4 pascal (24.6 psig) at 37°C generated by hermetic sealed dichlorofluoromethane -pressured bellows
Active Metering Mechanism	
Valve-accumulator subsystem	Electronically activated solenoid valves (2)
Accumulator pressure	8.4 x 10^4 pascal (12.3 psig) generated by hermetic sealed argon-pressured diaphragm
Accumulator stroke volume	Approx. 2 microliters
Material	Titanium, MP35N alloy, stainless steel, and silicone rubber

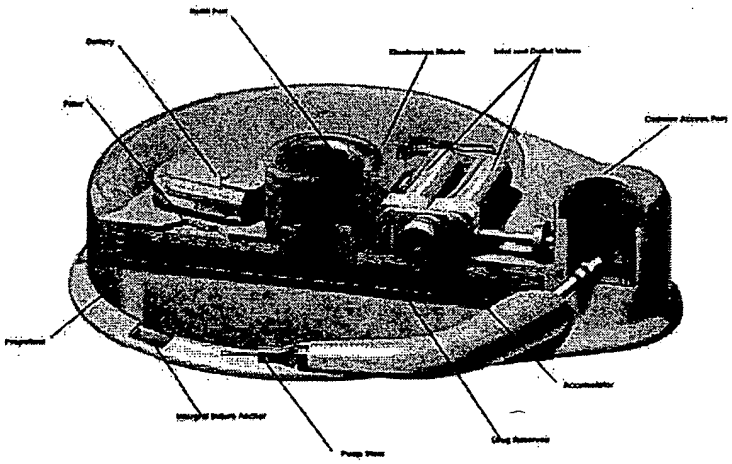
Prometra Programmable Infusion Pump System Description

The Flowonix Medical, Inc. Prometra Implantable Programmable Infusion Pump System consists of an Infusion Pump, Intrathecal Catheter and Programmable Pump Programmer.

The Prometra Implantable Programmable Infusion pump is a teardrop shaped metal container separated into three chambers by a welded metal bellows and base plate. The bellows serves as a flexible impermeable membrane that separates the pump's charging fluid from the drug reservoir. The base plate serves as a rigid substrate that separates the drug reservoir from the electronics and battery chamber. The metal bellows charging fluid chamber is permanently sealed and contained within the pump's lower outer housing. The space between the exterior of the bellows and outer housing serves as the propellant chamber. The propellant chamber contains a fluid that, at body temperature, is in a two phase state. Regardless of the chamber volume, the fluid remains in this two phase state and exerts a constant pressure on the bellows. The pressure exerted on the bellows is directly transmitted to the fluid in the drug reservoir, forcing expulsion of the drug from the reservoir into an electronically controlled flow metering valve-accumulator subsystem.

The flow rate of the pump is controlled by this valve-accumulator subsystem. The propellant pressure on the bellows forces the drug from the reservoir through a 0.22 µm filter to the first valve. When the pump electronics opens this valve, fluid passes into an accumulator in the valve-accumulator subsystem. Once the accumulator is filled as dictated by a predetermined period of time this valve closes sealing the reservoir from the accumulator. At the appropriate time a second valve opens, allowing a fixed volume of drug to flow from the accumulator through the catheter access port and into a silicone catheter for delivery to the selected body site. Figure 1 below shows a cross-section of the pump.

Figure 1: Pump Cross-section Showing Components



The design of the pump valve-accumulator subsystem enables the device flow rate to remain unaffected by anticipated changes in patient temperature and catheter exit variables (e.g., geographic location, air travel, etc.). This is accomplished through the precision design of the accumulator that limits the amount of fluid it can receive from the reservoir or expel to the catheter regardless of the pressure differentials it encounters during its normal operating environment.

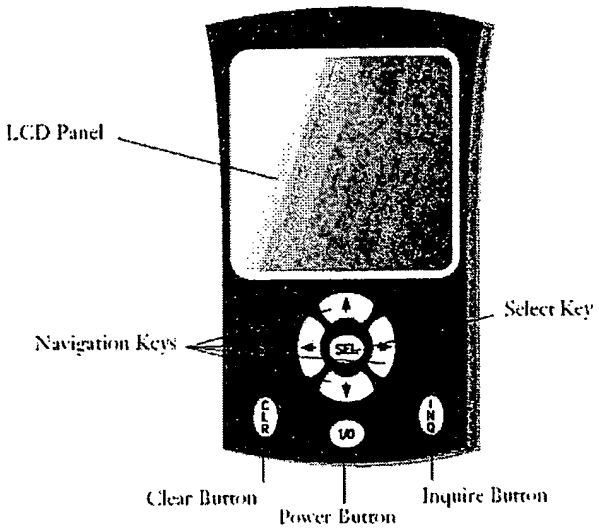
The teardrop shape of the pump is designed to help the clinician differentiate the catheter access port from the central drug chamber port after the pump is implanted. The drug chamber is refillable and is percutaneously accessed by means of the centrally located access port using a 22 gauge non-coring needle.

When the drug reservoir has been emptied (metal bellows collapsed), it can be refilled by percutaneous needle injection that penetrates the septum, a rubber self sealing membrane, and accesses the drug reservoir. Using a syringe, the drug is injected into the reservoir causing the metal bellows to expand. The expansion of the bellows simultaneously decreases the volume of the charging fluid chamber, causing the charging fluid vapor in the chamber to condense to its mostly liquid state, thus storing energy to move fluid from the drug chamber to the pumping system for the next flow cycle. This method of converting work to stored energy is reversible and precisely repeatable for each flow cycle. The percutaneous injection into the drug chamber refills the reservoir and recharges the unit for the subsequent flow cycle. The catheter access port is located on the periphery of the pump to allow for direct access to the catheter without interfering with the drug reservoir. The catheter access port is percutaneously accessed using a 20 gauge needle. The needle is designed such that if inadvertently inserted into the refill port, infusion is prevented. Conversely if the 22 gauge refill needle was inserted into the catheter access port infusion would also be precluded. The catheter access port can be used to evaluate catheter patency or catheter placement.

The pump is designed to be used with an attachable catheter. A catheter lock assembly allows the surgeon to attach the catheter to the pump after catheter placement. The Intrathecal Catheter serves as a conduit between the implanted Prometra Programmable Pump and the spinal intrathecal space. The catheter lock provides a means for securing the intrathecal catheter to a barbed stem protruding from the pumps external, flexible boot. Solutions expelled by the pump are delivered directly into the intrathecal space via the catheter, exiting via side holes located in the distal segment of the catheter wall.

A drug dosage regimen is programmed into the pump with a hand-held programmer (Figure 2). The design of the pump is such that it maintains a programmed flow profile over time throughout the therapy. This programmed flow profile may be reprogrammed if the patient's requirements change.

Figure 2: Programmer



Assembly, V53 Valve Set

Prepared By: Matthew Cunningham Date: 1/22/09

Approved By: John Klemm Date: 2/2/09
Engineering

Approved By: B Valentine Date: 2/3/09
Operations

Approved By: Roxana M. Hicks Date: 2/3/09
Quality

UNCONTROLLED COPY NOV 24 2009

TABLE OF CONTENTS

1.0 Purpose

The purpose of this document is to define the characteristics of the (V-53) valve assembly. The valve is intended to be used in a totally implantable, programmable drug delivery pump.

2.0 Scope

The scope of this document encompasses the pertinent characteristics of the (V-53) valve to be used in an implantable, programmable drug delivery pump. This document includes the basic physical, performance, safety and quality characteristics for the valve.

3.0 Description

The Valve Assembly consists of two dual port solenoid valves mounted to a titanium faceplate. The valves are open in an energized state and closed by a return spring in the de-energized state. The flow path is drug and bio-compatible.

4.0 Definitions

4.1 Ipo Pull Open Current - amount of current required to pull open the valve (in milliamps)

4.2 Iho Hold Open Current - the amount of current required to hold open the valve (in milliamps)

4.3 T_o Time Open - at a fixed Ipo, the amount of time for the valve to open (in milliseconds)

4.4 T_c Time Closed - after a fixed Iho, the amount of time for the valve to close (in milliseconds)

4.5 DCR DC Resistance of the valve coil (in ohms)

4.6 L Inductance of the valve coil (in henries)

4.7 IR Insulation Resistance between the valve case and coil obtained by measuring the leakage current at 50 Volts DC (in microamps at 50 volts)

4.8 PDA Percent Defective Allowable for lot acceptance

5.0 Reference Documents

5.1	DWG-0092-00924	Valves/Faceplate Assembly Mechanical Envelope Drawing
5.2	4C1079	WGL P/N for Valve Assembly
5.3	TM-0092-00987	Programmable Pump Solenoid Valve Evaluation Test
5.4	PPC-0092-01944	Product Performance Characteristics: InfuMedics Totally Implantable Programmable Infusion Pump
5.5	IPC-A-610D	Acceptability of Electronic Assemblies (replaces MIL-S-45743)

5.6	MIL-STD-202	Test Methods for Electronic and Electrical Parts
5.7	NEMA MW 1000 3-C	Magnet Wire (replaces J-W-1177)
5.8	ASTM B265	Titanium and Titanium Alloy Strip, Sheet and Plate
5.9	ASTM B348	Titanium and Titanium Alloy Bars and Billets
5.10	ASTM F67	Unalloyed Titanium for Surgical Implant Application

6.0 Physical Characteristics

6.1	Valve Assembly Envelope	Reference Attachment 1
6.2	Internal Volume	67µL/valve, 135ul/set (nominal)
6.3	Weight	4.76g wet (nominal), 4.69g dry (nominal)
6.4	Seat Elastomer	Dow MDX4-4210
6.5	Coil Face Diaphragm	CP Grade 4 Titanium
6.6	Return Spring	10.0 ± 0.5 grams
6.7	Filters	0.001 inch thick etched

No more then 10% of the etched filter holes may be obstructed do to incomplete etching

6.8	Filter Area (minimum)	0.077 inch diameter
6.9	Coil Potting	Centrifuge method
6.10	Electrical Leads	Insulated Wire, 26 AWG
6.11	Pole Button	AL29-4SS

7.0 Requirements

Valve assemblies shall meet all of the requirements specified herein, unless otherwise noted. Acceptance, in process, qualification, and characterization tests, along with the required test frequency, are defined in section 9.0. In the event of conflict between requirements of this specification and referenced documents, this specification shall govern.

7.1 Normal Operational Conditions

The device shall meet all of its performance and electrical characteristics, unless otherwise specified, over its operating life under the following operating conditions:

7.1.1	Operational Temperature Range	20°C to 41°C (68°F to 106°F)
7.1.2	Operational Pressure Range	6.5 to 43.0 psia
7.1.3	Operational Current	Refer to Section 7.3
7.1.4	Flow Direction	
	7.1.4.1 Inlet valve	Side to End Port
	7.1.4.2 Outlet valve	End to Side Port

7.1.5 Fluid Conditions

7.1.5.1 Type	Liquid, Gas, or Mixture (bubbles)
7.1.5.2 Fluid viscosity	Typical to water @ 37°C (98.6°F)
7.1.5.3 Salinity	0.9% Saline Solution

7.1.6 Resistance to Solvents

Per MIL-STD-202, method 215, except solvents shall be isopropyl alcohol and water. Solvent not applied to internal valve cavity.

7.1.7 Leak rate <.3µL/hr @ 25psid in the direction of flow

7.2 Performance Characteristics

The device shall meet the performance and electrical characteristics over the normal operating conditions specified in 7.1 throughout the operating life specified in 7.4.1. Exposure to extreme environments shall not cause the device to operate outside of its performance limits. Specific required tests shall be per section 10.0.

7.2.1 Seat Hermeticity	$1x10^{-6}$ atm cc/sec Helium maximum
7.2.2 Crack Open Pressure	
7.2.2.1 Side Port	80 psig minimum
7.2.2.2 End Port	32.5 psig minimum (25x1.3)
7.2.3 Flow Rate	> 600 µL/sec of water at 25psid (700 µL/sec goal)
7.2.4 Compliance	Not required

7.3 Electrical

7.3.1 Maximum Ratings: The device shall survive the following extreme conditions and shall meet its specified performance limits when subsequently operated under normal conditions. In addition to the following conditions, the device shall also be capable of passing the environmental tests of 7.4 & 7.5.

7.3.1.1 Voltage, Lead to Lead, applied either direction	25.0 VDC
7.3.1.2 Voltage, Case to Coil	50 Vrms
7.3.1.3 Voltage, Case to Coil	100.0 VDC
7.3.2 Voltage, Operational	3.0 to 6.0 VDC
7.3.3 Steady state pull open current (Ipo) (wet w/o pressure or dry)	
Manufactured	9.0 -16.5mA
Maximum over Life (1.83 million cycles)	16.5 mA
7.3.4 Steady state hold open current (Iho)	4.0mA minimum
(wet w/o pressure or dry)	8.8mA maximum
7.3.5 Pull open current @ 25 psid applied to side port	
Manufactured	9.0 -16.5mA
Maximum over Life (1.83 million cycles)	16.5 mA

7.3.6 Pulsed pull-open verification

Valve shall be verified to have pulled open when subject to the current pulse waveform, see TM-0092-00987.

7.3.7 DC Resistance 215 ± 20 ohms at 25°C

7.3.8 Inductance < 0.60 henries

7.3.9 Insulation Resistance (IR)

100 megohms (MΩ) minimum, coil to case, at 100 VDC ±10% and room temperature

7.3.10 Response Time

7.3.10.1	Open Time (t_o)	<10 msec. typical; 15 msec. max.
7.3.10.2	Close Time (t_c)	<20 msec. typical; 25 msec. max.

7.4 Environmental Conditions

The valve assemblies shall be capable of passing the following qualification tests. Unless otherwise specified, measurements before and after exposure shall include a visual inspection, DCR, L, IR, hermeticity, operating current, response times, and flow rate.

7.4.1 Expected Life (Years of Use): The operating life shall be ten years minimum under normal operating conditions (37°C @ 25 psid) at cycling rates of 1 Hertz or slower, to a minimum of 1.83 million accumulated cycles. The cycle life criteria of 1.83 million cycles is based on a minimum accumulator volume of 2.0 µL and a pump flowrate of 0.5 ml/day resulting in 250 valve cycles per day, which corresponds to 912.5 thousand cycles in the pump's ten year life. Multiplying by a safety factor of 2.0 results in a valve life criterion of 1.83 million cycles.

7.4.2 Life test: Valves shall be subject to pulse cycling at 37°C for a minimum of 1.83 million cycles with filtered (.80 um) bacteriostatic water or 0.9% saline flowing through the valve. Flow direction shall be side port to end port for the inlet valve and reverse for the outlet valve; fluid pressure shall be 25 psid. Pulsing rate shall be 1 Hertz or slower. Performance measurements shall be performed at a minimum of approximately ½, 1, and 1.83,million cycles.

7.4.3 Vacuum Bake: Non-operating, 60° ± 2°C (140° ± 4°F) for four hours minimum at one psia, device dry.

7.4.4 Storage Temperature (non-operating, device dry) -40°C to +60°C (-40°F to +140°F)

7.4.5 High Temp. Storage (non-operating, device dry) 60° ± 2°C (140° ± 4°F), 96 hours minimum

7.4.6 Low Temp. Storage (non-operating, device dry) -40° ± 2°C, (-40° ± 4°F), 96 hours minimum

7.4.7 Pressure Range (non-operating, device dry) 0 psia (30 millitorr) to 80 psig internal pressure, two minutes minimum

7.4.8 Thermal Shock: Non-operating, per MIL-STD-202, method 107, 130°C to -40°C (266°F to –40°F), 10 cycles

7.4.9 High Temperature / High Internal Pressure (simulated autoclave): Non-operating, 1.5 to 2.0 hours at 125°C (257°F) and 50-psig internal cavity pressure for five cycles

7.4.10 Vibration: Non-operating, per MIL-STD-202, method 204, condition C. Device mounting shall simulate pump base assembly

7.4.10.1 10 to 55 Hertz, 0.06 inch displacement, for 2 hours each axis

7.4.10.2 55 to 2,000 Hertz, 10 g's, for 35 minutes each axis

7.4.11 Mechanical shock

Non-operating per MIL-STD-202, method 213, condition C. Half-sine 100 g's peak, 6 ms duration, 3 shocks in each perpendicular direction, 18 shocks total. Device mounting shall simulate pump base plate.

7.5 Shipping and Handling

Unless otherwise specified, measurements before and after shipping and handling exposure shall include a visual inspection, DCR, L, IR, hermeticity, operating current, response times, and flow rate.

7.5.1 Expiration Period

V53 valves stored on site for 20 months or more following initial inspection must be reworked per RWRTR-0092-07441.

7.6 Design and Construction

7.6.1 Outline Dimensions: per Attachment 1

7.6.2 Markings: The valves assembly shall be marked with the manufacturer's identification, model and serial number. Markings shall remain legible after all tests.

7.6.3 Materials:

Materials shall be as specified. When a definite material is not specified, a suitable material shall be used which will enable the valves to meet the performance requirements over its intended life over the specified operating conditions. Acceptance or approval of any constituent material shall not be construed as a guarantee of acceptance of the finished product. Materials in contact with the drug path shall be in accordance with section 7.6.4.

7.6.3.1 Metals shall be corrosion resistant or plated or treated to resist corrosion when dissimilar metals are used in intimate contact with each other

Insulating materials, potting compounds, adhesives, plastics and tapes shall not degrade below minimum mechanical strength or insulation properties when subject to normal operating conditions specified throughout the valve operating life. Exposure to extreme environments shall not cause degradation in mechanical strength or insulation properties below minimum specified values.

7.6.4 Materials in Contact with the Drug Path

7.6.4.1 Metals in contact with the drug path shall be either unalloyed titanium per ASTM F67, ASTM B265, or ASTM B348, MP35N per ASTM F562 and 29-4SS per ASTM A276-98b (pole button) Metallic parts shall be passivated and cleaned.

7.6.4.2 Non-metallic material in contact with the drug path shall be (Dow Corning MDX4-4210 Clean Grade Elastomer) non-pyrogenic, non-toxic and shall meet the Class VI test requirements of U.S.P. 31.

7.6.5 Coil

The coil windings and electrical leads shall be completely insulated from the case and other grounded parts. Unless otherwise specified, the magnet wire shall conform to NEMA MW 1000 3-C. If because of size or temperature range, magnet wires conforming to NEMA MW 1000 3-C cannot be used, the selected wire shall be capable of meeting the inspection and test requirements of NEMA MW 1000 3-C.

7.7 Workmanship

Valves shall be manufactured, processed and tested in accordance with manufacturer's product assurance program per section 8.0. Valves shall be uniform in quality, cleanliness and free from cracked or deformed parts, sharp edges, burrs or other defects, which will affect performance, life or appearance.

7.7.1 Rework

All rework shall be done to baseline procedures and shall be documented as to insure traceability.

7.7.2 Cleanliness

Flow path shall be manufactured and tested in an environmentally controlled area.

7.8 Reliability

Devices supplied to this specification shall be qualified for long-term medical implant applications.

7.8.1 Magnetic Susceptibility

In an external magnetic field, the valves shall not pull open or be held open at field strength of less than 250 Gauss measured at the end of a valve. Value based on theoretical calculations performed on model and recorded in Infumedics report # TTR-0092-01634, analysis performed by Myatt Consulting, Inc. Physical confirmation is not required.

7.9 Electrical Leads

Pull strength shall not drop below minimum requirements after periods of high temperature exposure. Electrical leads bend strength shall not drop below the minimum requirements after periods of high temperature exposure. Electrical leads shall withstand a one-pound pull and bend test without evidence of loosening, rupturing or any degradation of the valve performance.

8.0 Inspection

8.1 In-Process Controls and Sample Inspection

The manufacturer's in-process inspections and controls shall be documented and baselined.

8.1.1 Fixtures and assemblies coming in contact with the flow path shall not generate particulate contamination. Fluids entering the valve shall be filtered with (.80 um or smaller) filter media; flow connections shall be corrosion resistant or passivated.

8.1.2 Weld set-up certification, consisting of sectioning and inspecting sample welds, shall be performed at the beginning of each shift and after any set-up change. Certification shall include sectioning and inspection of sample welds. Welds shall be 100% helium leak tested to 1×10^{-7} atm cc/sec and shall be 100% visually inspected under magnification for non-conformity, cracking or discoloration. Destructive Physical Analysis (DPA): Samples of various subassemblies shall be subject to a minimum of first and last weld sample evaluation

8.1.3 Solder joints shall be 100% inspected to baseline criteria prior to terminal potting. Electrical solder joints shall meet the requirements of IPC-A-610D or equivalent. When the design specifies a two-stage soldered lead (e.g. magnet wire to terminal, then terminal to lead wire), a higher melting point solder shall be used at the magnet wire joint. Solder flux shall be type R or RMA. Solder joints shall be cleaned to remove all traces of flux and contamination. Terminals and lead wires shall be solderable when tested per MIL-STD-202, method 208.

8.2 100 Percent Acceptance Test

8.2.1 Valve assemblies shall be subjected to 100 percent Acceptance Tests as follows:

Ipo Pull Open Current

Iho Hold Open Current

T_o Time Open

T_c Time Closed

DCR DC Resistance of the valve coil

L Inductance of the valve coil

IR Insulation Resistance between the valve case and coil

Helium Leak Test

9.0 Test Methods

9.1 Unless otherwise specified, the following general test conditions shall apply

9.1.1 Room Temperature

9.1.2 Fluid: filtered (.8um) bacteriostatic water (0.2% phenol, balance sterile water).

9.1.3 Fluid Pressure: 25 ± 0.5 psig.

9.1.4 Pulsing circuit, when specified.

9.1.5 Pressure and flow direction:

9.1.6 Inlet Valve: Side port to End port

9.1.7 Outlet Valve: End port to Side port

9.2 DC Resistance: Test method 303 of MIL-STD-202, correlated to 25°C. For copper conductor, use a temperature coefficient of resistance of 0.4 percent per °C.

9.3 Inductance: Series resistance method at 1 KHz.

9.4 Insulation Resistance (IR): Test method 302 of MIL-STD-202 at 100VDC.

9.5 Hermeticity of valve body (welds) and valve seats shall be measured with a helium mass spectrometer.

9.6 Operating Current: Pull-open (Ipo) and hold-open (Iho) currents shall be measured using the test set-up and waveform of TM-0092-00987 in the triangle wave mode output. Pulse Verification shall be checked using the test set-up of TM-0092-00987 with the test box in the pulse mode. Flow through the valve shall be verified.

9.7 Response Time: Open time (t_o) and close time (t_c) shall be measured using the test set-up and waveform of TM-0092-00987 in the square wave mode output.

9.8 Flow Rate: With 25 psid across the valve, measure the volume flowing per unit time.

9.9 Electrical leads strength: shall be determined by pull strength per MIL-STD-202, method 211A, test condition A, with a one-pound force. Bend testing shall be per MIL-STD-202, method 211A, testing condition B, with a one-pound force for three cycles.

10.0 Label and Packaging

Valve assemblies shall be individually packaged in suitable containers to prevent contamination, damage or degradation during transportation, handling and storage. Devices shall be supported in a manner which prevents undue stress on the terminal leads and the valve-to-face plate Welds. Devices shall be shipped completely dry.

11.0 Attachments

Attachment #1: DWG-0092-02124ATT1 – Assembly, V53 Valve Set

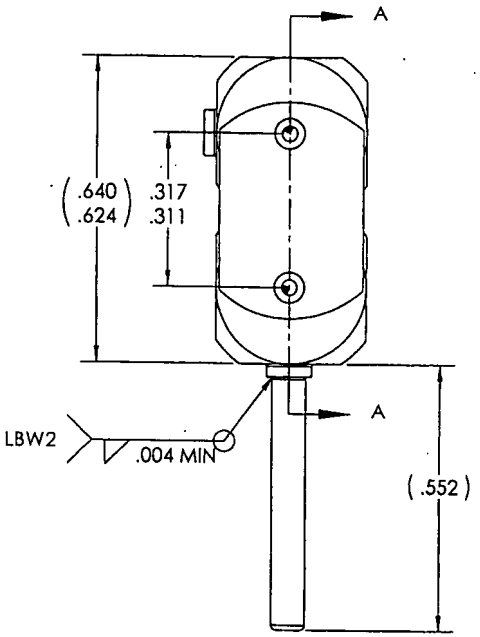
12.0 Revision Record

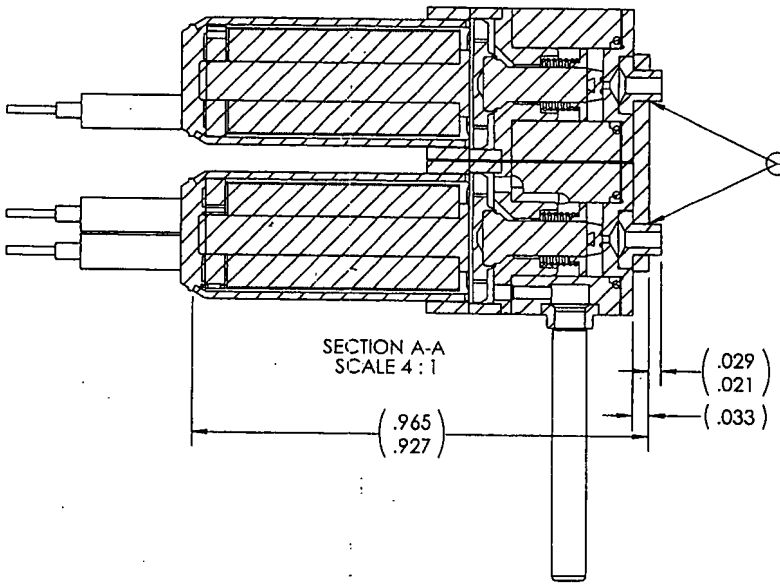
Rev.	Date	ECN	Description
Orig	7/11/08	08-0367	Original release
01	3/04/09	09-0016	Change 7.3.8, 7.3.9, 9.4, Removed 8.1.4

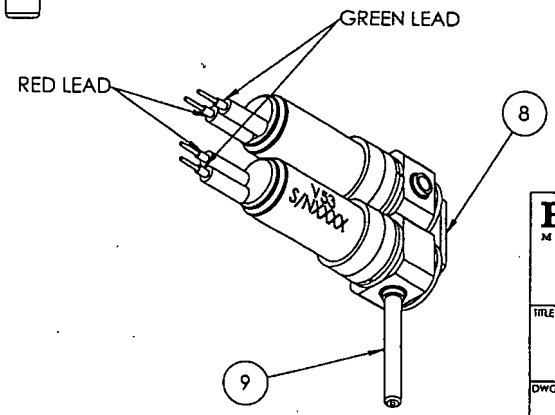
Attachment #1

DWG-0092-02124ATT1
Assembly, V53 Valve Set
(1 page)

ITEM NO.	PART NUMBER	DESCRIPTION	QTY.
N/A	DWG-0092-02113	Sub-Assembly, Final Closure	2
8	DWG-0092-02109	FACE PLATE	1
9	DWG-0092-02110	OUTLET TUBE	1







NOTES:

1. VENDOR MUST SUPPLY EACH OF THE FOLLOWING:
   - A. CERTIFICATE OF CONFORMANCE THAT ALL PARTS DELIVERED MEET THE REQUIREMENTS OF THIS SPECIFICATION. CERTIFICATE OF CONFORMANCE MUST INCLUDE PART NUMBER, REVISION, LOT NUMBER AND QUANTITY SHIPPED AT A MINIMUM.
   - B. METROLOGY REPORT WITH PICTURES OF INSPECTED SAMPLES CONFIRMING WELD PENETRATION/WELD INTEGRITY OR ACTUAL CROSS-SECTIONED SAMPLES FOR FIRST AND LAST PIECES.
2. VENDOR MUST NOTIFY PROVEN PROCESS OF ANY PROPOSED CHANGES TO SPECIFICATION, RAW MATERIALS, AND/OR MANUFACTURING PROCESS. NO CHANGES SHALL BE MADE WITHOUT WRITTEN APPROVAL FROM PROVEN PROCESS.
3. MATERIALS: PARTS TO BE SUPPLIED BY PROVEN PROCESS.
4. HANDLING REQUIRMENTS:
   - A. PARTS ARE TO BE HANDLED WITH TALC-FREE GLOVES AT ALL TIMES.
   - B. ALL WORK AREAS, TOOLING, AND FIXTURES MUST BE WIPED WITH ISOPROPYL ALCOHOL PRIOR TO USE.
   - C. HANDLE PARTS PER MP-0092-01271.
5. ASSEMBLY
   - A. ASSEMBLE PER MP-0092-02564 AND MP-0092-09108 (NOTE ORIENTATION OF SIDE PORT).
   - B. OPERATORS MUST BE TRAINED BY A QUALIFIED EMPOYEEE OF PROVEN PROCESS PRIOR TO PERFORMING THE ASSEMBLY AND WELD OPERATIONS.
6. PARTS TO BE DOUBLE POLY BAGGED/SEALED TO MAINTAIN CLEANLINESS AND PACKAGED IN A MANNER TO PREVENT DAMAGE DURING SHIPMENT. BAG TO BE IDENTIFIED WITH PART NUMBER, REVISION, LOT NUMBER, AND QUANTITY.

ProvenProcess MEDICAL DEVICES
141 Washington St
E Walpole MA 02032

TITLE	Assembly, V53 Valve Set
DWG	DWG-0092-02124ATT1
SIZE	B
REV	01
SCALE	4:1
SHEET	1 OF 1

EXHIBIT B

Assignment History for U.S. Patent No. 5,368,274

United States Patent and Trademark Office

Assignments on the Web > Patent Query

Patent Assignment Abstract of Title

NOTE:Results display only for issued patents and published applications. For pending or abandoned applications please consult USPTO staff.

Total Assignments: 8

Patent #: 5368274 **Issue Dt:** 11/29/1994 **Application #:** 07946392 **Filing Dt:** 09/17/1992

Inventors: THEODORE J. FALK, W. RICHARD BROWN, LAWRENCE E. MORRIS, NORBERT W. FRENZ JR.

Title: LOW POWER ELECTROMAGNETIC VALVE

Assignment: 1

Reel/Frame: 006263/0276 **Recorded:** 09/17/1992 **Pages:** 4

Conveyance: ASSIGNMENT OF ASSIGNORS INTEREST.

Assignors: FALK, THEODORE J. **Exec Dt:** 09/14/1992

BROWN, W. RICHARD **Exec Dt:** 09/15/1992

MORRIS, LAWRENCE E. **Exec Dt:** 09/14/1992

FRENZ, NORBERT W., JR. **Exec Dt:** 09/15/1992

Assignee: WILSON GREATBATCH LTD.
10,000 WEHRLE DRIVE
CLARENCE, NEW YORK 14031

Correspondent: MARTIN G. LINIHAN
HODGSON RUSS ANDREWS WOODS & GOODYEAR
INTELLECTUAL PROPERTY LAW GROUP
1800 ONE M & T PLAZA
BUFFALO, NY 14203

Assignment: 2

Reel/Frame: 007405/0497 **Recorded:** 03/27/1995 **Pages:** 4

Conveyance: ASSIGNMENT OF ASSIGNORS INTEREST (SEE DOCUMENT FOR DETAILS).

Assignor: WILSON GREATBATCH LTD. **Exec Dt:** 02/15/1995

Assignee: STRATO/INFUSAID INC.
1400 PROVIDENCE HIGHWAY
NORWOOD, MASSACHUSETTS 02062

Correspondent: PFIZER INC
DR. PETER C. RICHARDSON
235 EAST 42ND STREET, 20TH FLOOR
NEW YORK, NY 10017-5755

Assignment: 3

Reel/Frame: 008579/0381 **Recorded:** 06/30/1997 **Pages:** 6

Conveyance: ASSIGNMENT OF ASSIGNORS INTEREST (SEE DOCUMENT FOR DETAILS).

Assignor: STRATO/INFUSAID, INC. **Exec Dt:** 06/18/1997

Assignee: PROGRAMMABLE PUMP TECHNOLOGIES, INC.
235 EAST 42ND STREET
NEW YORK, NEW YORK 10017

Correspondent: PFIZER, INC.
PETER C. RICHARDSON
235 EAST 42ND STREET
20TH FLOOR
NEW YORK, NY 10017-5755

Assignment: 4

Reel/Frame: 008698/0956 **Recorded:** 09/16/1997 **Pages:** 10

Conveyance: ASSIGNMENT OF ASSIGNORS INTEREST (SEE DOCUMENT FOR DETAILS).

Assignor: STRATO/INFUSAID INC. **Exec Dt:** 06/18/1997

Assignee: PROGRAMMABLE PUMP TECHNOLOGIES, INC.
235 EAST 42ND STREET
NEW YORK, NEW YORK 10017

Correspondent: HODGSON, RUSS, ANDREWS, WOODS & GOODYEAR
MARTIN G. LINIHAN, ESQ.
INTELLECTUAL PROPERTY LAW SECTION
1800 ONE M&T PLAZA
BUFFALO, NY 14203

Assignment: 5

Reel/Frame: 017400/0899 **Recorded:** 12/30/2005 **Pages:** 8

Conveyance: ASSIGNMENT OF ASSIGNORS INTEREST (SEE DOCUMENT FOR DETAILS).

Assignor: PROGRAMMABLE PUMP TECHNOLOGIES, INC. **Exec Dt:** 08/16/2005

Assignee: INFUMEDICS, INC.
141 WASHINGTON STREET
EAST WALPOLE, MASSACHUSETTS 02032

Correspondent: NIELDS & LEMACK
176 E. MAIN STREET
SUITE 7
WESTBORO, MA 01581

Assignment: 6

Reel/Frame: 021701/0484 **Recorded:** 10/14/2008 **Pages:** 4

Conveyance: ASSIGNMENT OF ASSIGNORS INTEREST (SEE DOCUMENT FOR DETAILS).

Assignor: INFUMEDICS, INC. **Exec Dt:** 10/09/2008

Assignee: INSET TECHNOLOGIES INCORPORATED
500 INTERNATIONAL DRIVE - SUITE 141
MT. OLIVE, NEW JERSEY 07828

Correspondent: NIELDS & LEMACK
SUITE 5
176 E. MAIN STREET
WESTBORO, MA 01581

Assignment: 7

Reel/Frame: 024547/0039 **Recorded:** 06/16/2010 **Pages:** 4

Conveyance: CHANGE OF NAME (SEE DOCUMENT FOR DETAILS).

Assignor: INSET TECHNOLOGIES INCORPORATED **Exec Dt:** 03/23/2010

Assignee: MEDASYS INCORPORATED
500 INTERNATIONAL DRIVE
SUITE 200
MOUNT OLIVE, NEW JERSEY 07828

Correspondent: ERIC T. KRISCHKE
ONE METROPOLITAN SQUARE
SUITE 2600
ST. LOUIS, MO 63102

Assignment: 8

Reel/Frame: 028023/0921 **Recorded:** 04/10/2012 **Pages:** 3

Conveyance: CHANGE OF NAME (SEE DOCUMENT FOR DETAILS).

Assignor: MEDASYS INCORPORATED **Exec Dt:** 02/24/2012

Assignee: FLOWONIX MEDICAL INCORPORATED
500 INTERNATIONAL DRIVE
SUITE 200
MOUNT OLIVE, NEW JERSEY 07828

Correspondent: THE MARBURY LAW GROUP PLLC
11800 SUNRISE VALLEY DRIVE
15TH FLOOR
RESTON, VA 20191

Search Results as of: 08/29/2012 09:37 AM

If you have any comments or questions concerning the data displayed, contact PRD / Assignments at 571-272-3350. v.2.3.2
Web interface last modified: July 10, 2012 v.2.3.2

EXHIBIT C

Copy of U.S. Patent No. 5,368,274

US005368274A

United States Patent [19]

Falk et al.

[11] Patent Number: 5,368,274

[45] Date of Patent: Nov. 29, 1994

[54] **LOW POWER ELECTROMAGNETIC VALVE**

[75] Inventors: **Theodore J. Falk**, Clarence; **W. Richard Brown**, Clarence Center; **Lawrence E. Morris**, Bowmansville; **Norbert W. Franz, Jr.**, Clarence, all of N.Y.

[73] Assignee: **Wilson Greatbatch Ltd.**, Clarence, N.Y.

[21] Appl. No.: **946,392**

[22] Filed: **Sep. 17, 1992**

[51] **Int. Cl.**[5] **F16K 31/04**

[52] **U.S. Cl.** **251/129.16**; 251/129.17

[58] **Field of Search** 251/129.16, 129.17, 251/129.18, 129.21; 335/260

[56] **References Cited**

U.S. PATENT DOCUMENTS

2,697,581	12/1954	Ray	251/129.17
3,406,715	10/1968	Hruby, Jr.	137/550
4,196,751	4/1980	Fischer	251/129.16
4,390,130	6/1983	Linssen	251/129.16
4,541,429	9/1985	Prosl	251/129.21
4,621,660	11/1986	Klocke	251/129.09
4,714,234	12/1987	Falk	251/129.17
4,858,956	8/1989	Taxon	251/129.18
4,936,337	5/1990	DuHack	251/129.15

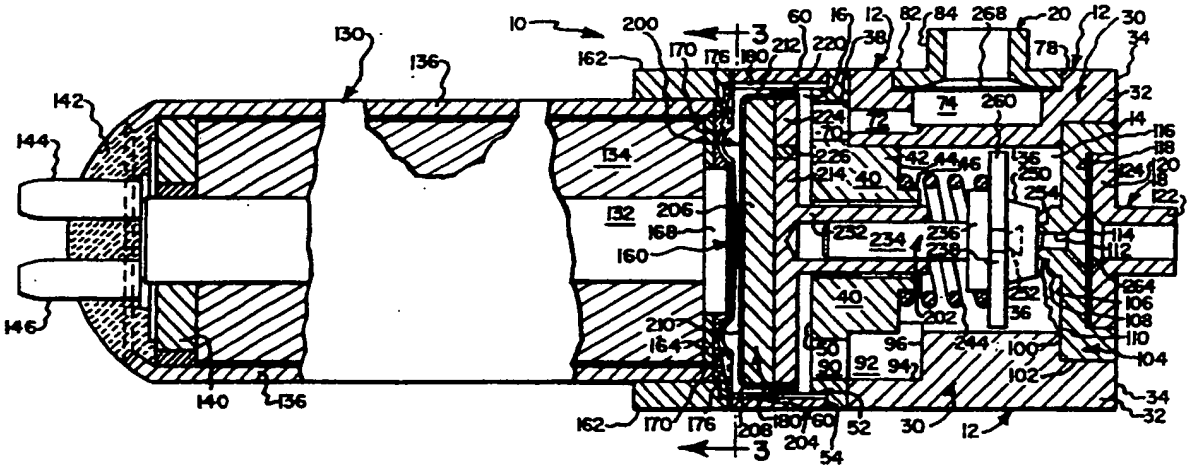
Primary Examiner—Robert G. Nilson

Attorney, Agent, or Firm—Hodgson, Russ, Andrews, Woods & Goodyear

[57] **ABSTRACT**

An electromagnetic valve comprising a housing having a fluid containing region and first and second ports in communication with the region, an electromagnet carried by the housing located external to the fluid containing region, and a thin diaphragm of fluid impermeable material which hermetically isolates the electromagnet from the fluid containing region. An armature is movably positioned in the region and has a pole portion located for magnetic attraction by the electromagnet and has a plunger portion provided with a valve formation for opening and closing one of the ports to place both ports in fluid communication through the fluid containing region of the housing and to block fluid communication between the ports. The armature is moved from a rest position through a forward stroke when attracted by the electromagnet to change the control state of the valve, and the armature is moved by a biasing spring in an opposite direction through a return stroke back to the rest position. The armature pole portion is of a material selected to achieve a desirable balance between fluid compatibility and magnetic properties for rapid and effective valve operation. Passages in the barrier and the armature pole portion allow the rapid valve movement and accommodate bubbles in the fluid, the armature is provided with structure for effectively guiding the same, and a valve seat structure resists fluid leaks.

28 Claims, 2 Drawing Sheets



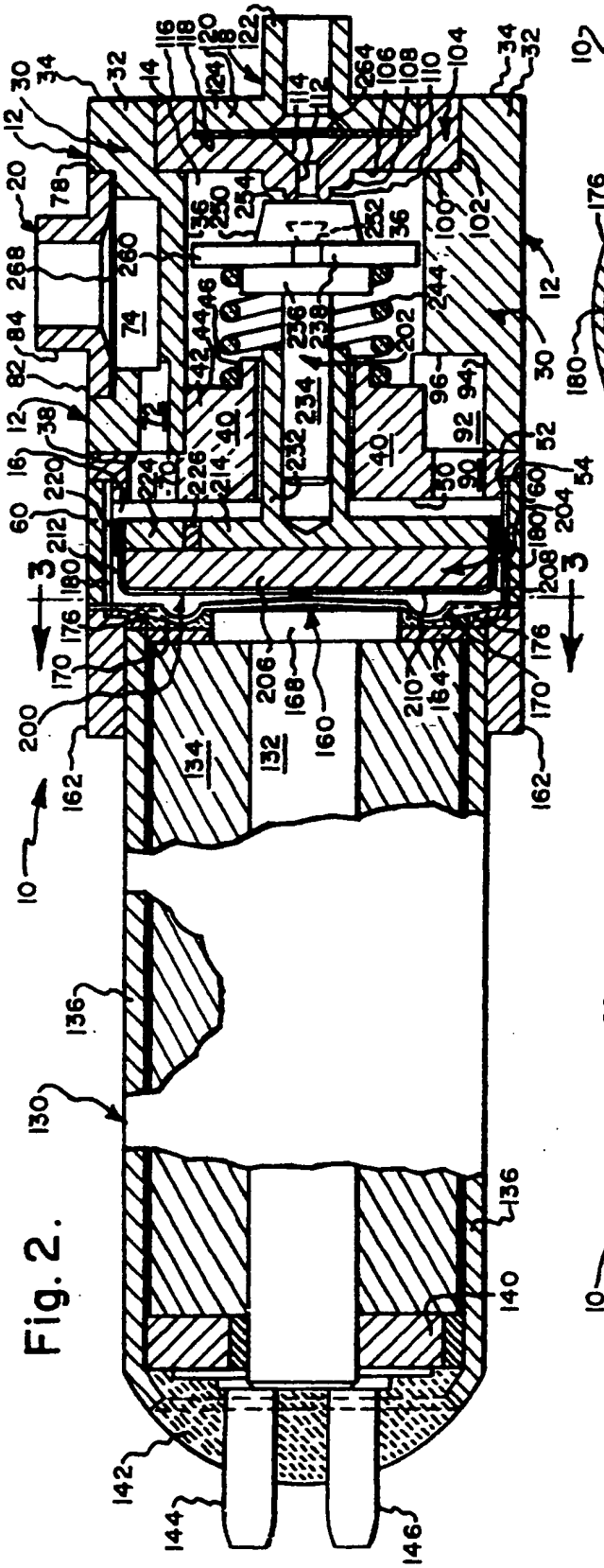


Fig. 2.

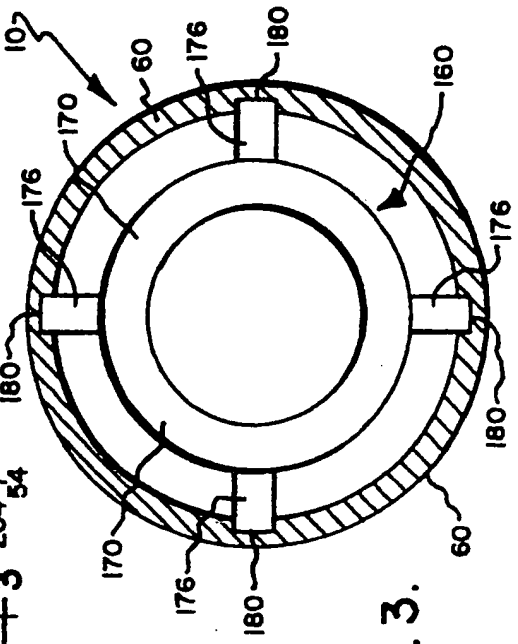


Fig. 3.

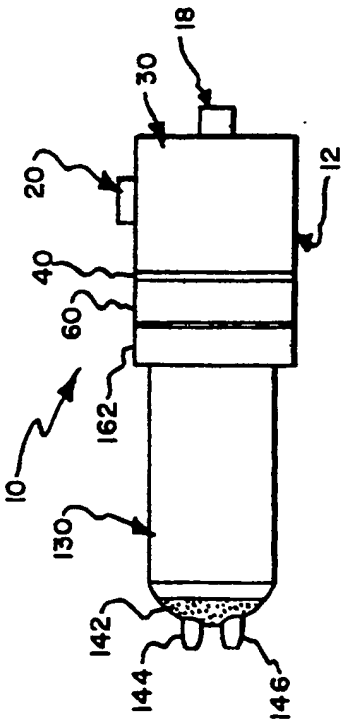


Fig. 1.

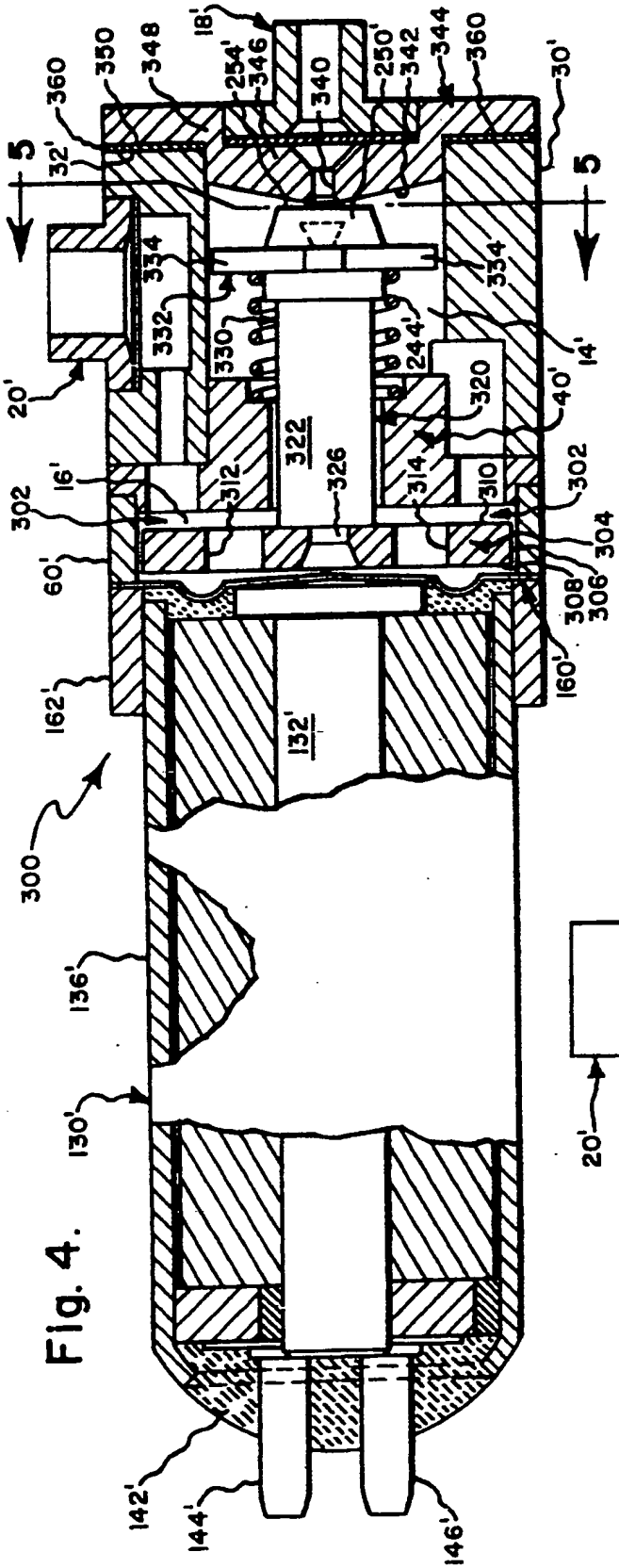

18'
254'
346
348
350
360
340
250'
342
344
360
30'
5
32'
5
334
332
330
244'
14'
20'
320
40'
322
16'
312
326
314
310
302
302
304
60'
308
306
160'
162'
132'
300
136'
130'
142'
144'
146'

Fig. 4.

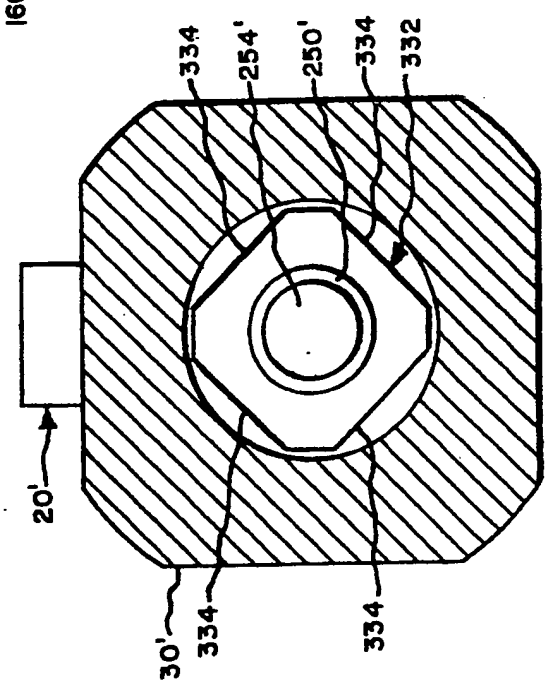

334
254'
250'
334
332
20'
30'
334
334

Fig. 5.

LOW POWER ELECTROMAGNETIC VALVE

BACKGROUND OF THE INVENTION

This invention relates to the art of electromagnetically-operated fluid valves, and more particularly to a new and improved electromagnetic valve which operates at extremely low power for use in implantable fluid delivery systems.

The principal requirements for a valve in such fluid delivery systems are low power drain, since the valve must be driven by an implanted battery, and compatibility with the drug being handled. Additional considerations include optimum magnetic characteristics of certain valve components, improved reliability and reduced cost. It would, therefore, be highly desirable to provide an electromagnetically-operated valve which is safe, reliable, light in weight, small in size, which operates without excessive demand on the available energy supply and which is compatible with drugs or similar liquids being handled. It also would be advantageous to provide such a valve which achieves a desirable balance between drug compatibility of component material and electromagnetic properties of that material, which insures rapid and effective closing of the valve, which accommodates bubbles in the fluid, which is resistant to fluid leaks, which provides effective guiding of moving valve components and which is relatively easy to assemble.

SUMMARY OF THE INVENTION

It is, therefore, a primary object of this invention to provide a new and improved electromagnetically-operated valve for use in implantable fluid delivery systems.

It is a more particular object of this invention to provide such a valve which operates at extremely low power levels.

It is a further object of this invention to provide such a valve which is compatible with drugs and similar liquids being handled.

It is a further object of this invention to provide such a valve which achieves a desirable balance between fluid compatibility and electromagnetic properties of material of valve components.

It is a more particular object of this invention to provide such a valve which features rapid opening and closing, resists fluid leaks, accommodates bubbles in the fluid and provides effective guiding of moving valve components.

It is a further object of this invention to provide such a valve which is small in size, light in weight, relatively easy to assemble and reliable in operation.

It is a further object of this invention to provide such a valve which is electrically and magnetically efficient.

The present invention provides an electromagnetic valve comprising a housing having a fluid containing region and first and second ports in communication with the region, electromagnet means carried by the housing located external to the fluid containing region of the housing, and barrier means in the form of a thin diaphragm of fluid impermeable material which hermetically isolates the electromagnet from the fluid containing region. An armature is movably positioned in the region and has a pole portion located for magnetic attraction by the electromagnet means and has a plunger portion provided with valve means for opening and closing one of the ports to place both ports in fluid communication through the fluid containing region of the housing in one control state of the valve and to block fluid communication between the ports in another control state of the valve. The armature is moved from a rest position through a forward stroke when attracted by the electromagnet means to change the control state of the valve, and the armature is moved by biasing means in an opposite direction through a return stroke back to the rest position. The armature pole portion has a lateral dimension several times greater than the longitudinal dimension thereof and is of a material selected to achieve a desirable balance between fluid compatibility and magnetic properties for rapid and effective valve operation. Passage means in the barrier means and the armature pole portion allow for rapid valve movement and accommodate bubbles in the fluid, the armature is provided with means for effectively guiding the same and a valve seat structure resists fluid leaks. A magnetic circuit is defined including the electromagnet means, the armature pole portion, a portion of the barrier means and a gap between the pole portion and the electromagnet means located in the fluid containing region of the housing and external to the electromagnet means. The gap is closed in response to electrical energization the electromagnet means to move the armature and change the control state of the valve. The valve is made electrically and magnetically efficient by minimizing the total gap within the magnetic circuit, by having the pole face area relatively large on the armature pole portion and by having the electromagnet include a coil on a core of relatively small diameter.

The foregoing and additional advantages and characterizing features of the present invention will become clearly apparent upon a reading of the ensuing detailed description together with the included drawing wherein:

BRIEF DESCRIPTION OF THE DRAWING FIGURES

FIG. 1 is a side elevational view of a valve according to the present invention;

FIG. 2 is an enlarged longitudinal sectional view, partly in elevation, of the valve of FIG. 1 and illustrating one embodiment of the present invention;

FIG. 3 is a sectional view taken about on line 3—3 in FIG. 2;

FIG. 4 is a view similar to FIG. 2 illustrating a valve according to another embodiment of the present invention; and

FIG. 5 is a sectional view taken about on line 5—5 in FIG. 4.

DETAILED DESCRIPTION OF THE ILLUSTRATED EMBODIMENT

Referring now to FIGS. 1–3, a valve 10 according to one embodiment of the present invention includes a housing 12 which is generally hollow, either rectangular or cylindrical in overall shape, and valve 10 includes an interior region for containing fluid, i.e. the liquid to be delivered. As shown in FIG. 2 the hollow interior region is divided in a manner which will be described into a first chamber 14 and a second chamber 16 in fluid communication therewith. There is a first port generally designated 18 in fluid communication with the first chamber and adapted to be connected in the fluid handling circuit. There is also a second port 20 in fluid communication with the second chamber 16 and

adapted to be connected in the fluid handling circuit. In the illustrative valve shown, port 20 is connected to the relatively higher pressure portion of the circuit, and port 18 is connected to the relatively lower pressure portion. Thus, port 20 may be viewed as the valve inlet and port 18 as the valve outlet. By way of example, in an illustrative implanted drug delivery system incorporating valve 10, the inlet and outlet 20 and 18, respectively, would be connected in a fluid circuit between a drug supply or reservoir and an outlet catheter for delivering the drug to the body site.

As shown in FIG. 2, housing 12 is generally hollow including a body portion 30 of relatively substantial wall thickness. Housing 12 also includes a first axial end portion 32 extending from one end of body 30, i.e. the right-hand end as viewed in FIG. 2, and which is of relatively smaller wall thickness terminating in an axial end face 34. Housing portion 30 defines an interior region of constant diameter having an inner surface 36. The housing portion 30 terminates at the other end thereof, i.e. the left-hand end as viewed in FIG. 2, in an end face 38.

Housing 12 further comprises a spring retainer element 40 in the form generally of a bushing having outer dimensions substantially equal to the outer dimensions of body portion 30 so as to be substantially flush therewith. Element 40 includes an axial extension 42 having an outer diameter substantially equal to the inner diameter of the body portion 30 so as to be received therein in a tight friction-like fit. Extension 42 terminates in an annular shoulder defined by axial and cylindrical surfaces 44 and 46, respectively, for providing a spring retaining function in a manner which will be described. The opposite end of element 40 terminates in an axial end face 50. An annular shoulder is defined by cylindrical and axial surfaces 52 and 54, respectively, at the peripheral junction between end face 50 and the outer surface of body 30. The shoulder receives one end of a first weld ring element 60 having an outer diameter substantially equal to the outer dimensions of element 40 so as to be substantially flush therewith. Ring element 60 is welded at the one end thereof, i.e. the right-hand end as viewed in FIG. 2, to element 40 at the aforementioned shoulder thereof in a suitable manner. Ring 60 is joined at the opposite end thereof to other components of the pump housing in a manner which will be described.

Chamber 16 is placed in fluid communication with port 20 in the following manner. A first longitudinal bore or passage 70 is provided in the body of retainer element 40, extending axially inwardly from end face 50, and a second longitudinal bore or passage 72 is provided in housing body portion 30 located so as to be open at one end to passage 70 and to be near port 20 at the other end thereof. A generally cylindrical chamber 74 is provided in housing body portion 30 in registry with port 20 and located so that the other end of passage 72 opens into the annular or circumferential wall of chamber 74. The one axial end of chamber 74 is defined by an internal surface in body portion 30. The opposite axial end of chamber 74 is open to port 20 and is circumscribed by an annular recess defining a ledge 78 which engages an annular rim 82 of a tubular fitting 84 which defines port 20. In the arrangement shown, the longitudinal axes of chamber 74 and fitting 84 are substantially coincident. The fitting 84 defining port 20 is adapted for connection to a conduit such as a flexible tubing comprising a portion of the afore-mentioned fluid circuit.

Thus, chamber 16 is placed in fluid communication with port 20 via the arrangement of passages 70 and 72 and chamber 74. Chamber 16 is placed in fluid communication with chamber 14 in the following manner. Another longitudinal bore or passage 90 is provided in the body of retainer element 40, extending axially inwardly from end face 50 and located substantially diametrically opposite the passage 70. Body portion 30 is provided with a recess 92 in the lower portion of the wall thereof as viewed in FIG. 2 and located so as to be in fluid communication with passage 90. Recess 92 is defined by an axially extending surface 94 and a radially extending surface 96 leading from surface 92 to the inner wall surface of body portion 30. As a result, the interior of body portion 30, and thus chamber 14, is placed in fluid communication with chamber 16 via the arrangement of passage 90 and recess 92.

Port 20 is provided by the following arrangement. A cylindrical recess of short axial length is provided in housing axial end face 34 and terminates in an inner annular end face 100. The inner surface 102 of the recess has a diameter larger than that of housing inner surface 36. Surfaces 100 and 102 define an annular shoulder which receives the cylindrical body of a ferrule element 104 in a tight-fitting relationship. Ferrule 104 has an inner axial end face 106 exposed to the housing interior region and is provided with a central, boss-like axial extension 108 having an axial end face provided with an annular valve seat formation 110 which is shaped to define a sharp annular edge facing axially into the housing interior region. A central bore or passage 112 of constant diameter extends axially inwardly from valve seat formation 110 whereupon it meets a passage 114 of increasing diameter. Ferrule 104 also has an outer axial end face 116 which meets housing end face 34 in a substantially flush relationship. A cylindrical recess 118 is formed in end face 116 and extends inwardly for about half the axial length of ferrule 104. A fitting 120 having a cylindrical portion 122 and an annular flange or lip 124 is received in recess 118. In particular, the outer diameter of lip 124 is substantially equal to the diameter of recess 118 to provide a tight fit. The axial length of lip 124 is substantially equal to the axial length of recess 118 so that the outer annular surface of lip 124 is substantially finish with ferrule end face 116. Thus, a flow path is defined through the central passage of fitting 120 and the passage portions 112 and 114.

By way of example, in an illustrative valve, housing 12 and the port fittings 84 and 120 all are of metal, and for a drug delivery valve for implantation in a patient, titanium has been formed to provide satisfactory results. In such an illustrative valve, housing 12 has an overall length of 0.36 inch measured between the axial end face 34 of body portion 30 and the outer axial end face of weld ring element 60. The inner surface 36 of housing body portion 30 has a diameter of 0.17 inch, and body portion 30 has an outer dimension of 0.31 inch. Passages 70 and 72 have diameters of 0.038 inch and 0.020 inch, respectively. Chamber 74 has an inner diameter of 0.12 inch and an axial length of 0.031 inch, and fitting 84 has an inner diameter of 0.062 inch. Passage 90 has a diameter of 0.038 inch. Passage 112 has a diameter of 0.015 inch, passage 114 has a maximum diameter of 0.055 inch, and fitting 120 has an inner diameter of 0.032 inch.

The valve of the present invention further comprises electromagnet means generally designated 130 carried by housing 12 and located external to the fluid containing region of the housing. As shown in FIG. 2 the elec-

tromagnet 130 includes a core 132 in the form of a spool which is generally solid cylindrical in shape. A coil 134 is wound on spool 132 and contained within a hollow housing 136 generally cylindrical in shape. One end of electromagnet 130 is adjacent and in abutting relation to housing 12 and the opposite end, i.e. the left-hand end as viewed in FIG. 2 is closed by an arrangement including a washer 140 and a body 142 of encapsulant such as expoxy material. A pair of terminals 144,146 provide electrical connection from a power source, such as a lithium battery charging circuit and capacitor, to electromagnet 130. Electromagnet 130 is joined to housing 12 in the following manner.

The interior, fluid containing region of housing 12 and the electromagnet 130 are separated by a barrier means of fluid impervious material in the form of a relatively thin plate or diaphragm-like component 160. A second weld ring 162 is provided on the end of magnet housing 136 adjacent housing 12. The outer diameter of ring 162 is substantially equal to the outer diameter of the first weld ring 60 so that the respective outer surfaces are substantially flush. The region between coil 134 and barrier 162 is filled with epoxy or like material generally designated 164. The housing and electromagnet structures are placed in abutting relation on opposite sides of the plate 160, and the assembly is secured together by a weld joining the respective outer surfaces of the weld rings 60 and 162. In addition, an enlarged annular end portion 168 of spool 132 contacts the central portion of plate 160 in a manner supporting the same. In accordance with the present invention, the central portion of barrier means or plate 160 is shaped in a manner to improve the operation of valve 10 during closing thereof in a manner which will be described. Plate 160 is formed with an annular groove or depression 170 in the surface facing housing 12 and having an inner diameter substantially equal to the outer diameter of spool end 168 to receive end 168 therein and strengthen plate 160.

In accordance with the present invention, barrier 160 also is formed with passage means generally designated 176 along the surface facing housing 12 for a purpose to be described. According to a preferred mode of the present invention as illustrated in FIG. 3, barrier means 160 is provided with four passage means or channels 176 at 90 degree angular increments around the circumference of barrier 160. Each passage means or channel 176 extends in a radial direction between groove 170 and the periphery of barrier plate 160. There is also provided, in accordance with the present invention, longitudinally extending passage means 180 formed in the housing inner surface for co-operating with the passage means 176 on the barrier means 160. In particular, the longitudinally extending passage means 180 are provided along the inner surface of weld ring 60, and as shown in FIG. 3. There are four passages 180 in circumferential registry or alignment with the channels 176. The role of the channels 176 and passages 180 in the operation of valve 10 will be described in detail presently.

By way of example, in an illustrative valve, spool 132, magnet housing 136 and washer 140 are of ferromagnetic material, preferably 4750 nickel iron alloy. Plate 160 and weld rings 60 and 162 are of titanium. Spool 132 has a length of about 0.56 inch and a diameter of about 0.10 inch. Housing 136 has a wall thickness of about 0.015 inch, rings 60 and 162 have thicknesses of about 0.016 inch and 0.024 inch, respectively, and diaphragm 160 has a thickness of about 0.001 inch. Coil 134 comprises about 4580 turns of 43 gauge wire.

The valve according to the present invention further comprises an armature generally designated 200 positioned in the fluid containing region of housing 12. The armature has a pole portion located for magnetic attraction by the electromagnet 130, a plunger portion in the chamber 16 and a valve portion for opening and closing port 18. The armature 200 is movably supported in housing 12 for movement from a rest position through a forward stroke when attracted by the electromagnet 130 to open port 18 to place the ports 18 and 20 in fluid communication through the chambers 14, 16 and for movement in an opposite direction through a return stroke back to the rest position closing port 18 and blocking fluid communication between ports 18,20 through chambers 14,16. In FIG. 2, armature 200 is shown in the rest position at the end of the return stroke.

Armature 200 includes a shaft or rod portion 202 which is positioned in housing 12 with the longitudinal axis thereof generally coincident with the longitudinal axis of housing 12. A major portion of the length is a section of relatively small diameter. Armature 200 includes a pole portion generally designated 204 which occupies a major portion of chamber 16 in which it is located, and pole portion 204 has a lateral dimension as viewed in FIG. 2 which is several times greater than the longitudinal dimension thereof. In accordance with the present invention, pole portion 204 comprises a body of magnetic material within a titanium enclosure, the encapsulation provided by the titanium enclosure providing protection against corrosion from insulin stabilized for use in implantable delivery systems and other corrosive drugs. In particular, pole portion 204 comprises a body 206 in the form of a disc. The enclosure comprises a thin-walled cap 208 having a base 210 contacting one axial face of disc 206 and an annular rim 212 contacting the periphery of disc 206. The enclosure is completed by a disc-shaped body 214 contacting the opposite axial end face of disc 206 and abutting the rim 212 of cap 208. As shown in FIG. 2, rim 212 of cap 208 extends slightly axially beyond the periphery of disc 206, body 214 fits within and contacts rim 212 and a weld ring 220 embraces the periphery of rim 212 so that ring 220, rim 212 and the disc-shaped body 214 can be welded together at the junctions thereof.

The disc-shaped body 214 is provided with at least one vent passage 224 therein to evacuate residual gas during assembly, the passage 224 being sealed by a plug 226 after assembly. Passage 224 is in the form of an axially extending through bore in body 214. The provisions of passage 224 and plug 226 is necessary because the small residual volume of gas within cup 208 must be evacuated to hold cup 208 tight against disc 206 even when the interior of valve 10 is at low pressure. Plug 226 is in the form of a filler pin and is welded in place with the entire assembly under vacuum to close the vent hole 224 in body 214.

By way of example, in an illustrative valve, disc 206 has a diameter of about 0.27 inch, an axial length of about 0.035 inch and is of 4750 nickel-iron alloy, body 214 has a diameter of about 0.27 inch, an axial length of about 0.14 inch and is of titanium, and cap 208 has a wall thickness of about 0.001 inch and is of titanium. The 4750 nickel-iron alloy has a relatively high saturation flux density. Weld ring 220 has a thickness of about 0.005 inch and is of titanium. Weld ring 220 facilitates

welding the thin material of cup **208** by sandwiching it between ring **220** and disc-shaped body **214** and then making a laser weld.

Thus, the armature pole portion **204** terminates at the end facing electromagnet **130** in an axial end face which serves as the pole face and is disposed substantially perpendicular to the armature axis. The armature pole face together with electromagnet **130** define the magnetic circuit gap which is closed during the forward armature stroke. The pole face is of relatively large cross-sectional area as compared to the cross sectional area of the armature shaft portion **202**. The armature pole portion **204** serves as the plunger portion of the armature, and as the pole face moves toward plate **160** when magnet **130** is energized, pole portion **204** upon moving in chamber **16** displaces fluid and moves it toward chamber **14**.

Armature shaft portion **202** is joined to the pole portion **204** via a sleeve-like axial projection or bushing **232** extending from disc-shaped body **214** to which is attached an armature rod or shaft **234**. The outer diameter of bushing **232** is slightly smaller than the inner diameter of retainer element **40** so that bushing **232** is freely longitudinally movable along within retainer **40**. The attachment is made by crimping the bushing **232** which allows the length of the plunger assembly to be changed to adjust the plunger stroke. Shaft **234** is provided with an enlargement at the end opposite bushing **232** which includes two relatively larger diameter shaft sections. In particular, there is a first section **236** facing bushing **232** and a second, axially adjacent section **238** which is of larger diameter. The two sections are of relatively short axial length and they define therebetween a shoulder facing pole portion **204**.

There is provided biasing means in the form of a coil spring **244** for urging armature **200** toward the rest position shown in FIG. 2. One end of spring **244** seats in the annular shoulder defined by the armature shaft sections **236,238**. The opposite end of spring **244** seats in the annular shoulder defined by surfaces **44,46** of retainer element **40** previously described. Retainer **40** is concentric with the armature shaft portion **202** and receives spring **244** which also is concentric with armature shaft portion **202**. As previously described, the armature shaft portion **202**, in particular bushing **232**, is freely axially movable within retainer **40**.

Armature **200** has a valve portion at the axial end of the armature opposite that of the pole face portion **204** for closing the port **18** when the armature is in the rest position and for opening port **18** when the armature is moved during the forward pumping stroke. There is provided a valve element **250** in the form of a body of elastomer material having a frustoconical shape with the larger diameter axial end face thereof abutting the outer axial end face of armature shaft section **238**. Element **250** is secured to shaft section **238** by a fastener in the form of a conical key designated **252**. Element **250** has an outer flat axial end face **254** adapted to sealing contact the annular valve seat formation **110** in the closed condition or state of the valve as shown in FIG. 2. Element **250** preferably is of silicone rubber which provides a relatively soft valve seat more resistant to fluid leaks.

By way of example, in an illustrative valve, the armature rod or shaft **234** and the enlargement defined by the two sections **236,238** are machined from metal, preferably titanium. The overall length between the end of shaft **234** within bushing **232** to outer face of section **238** is about 0.17 inch. The outer diameter of shaft **234** is about 0.036 inch, the inner diameter of retainer **40** is about 0.073 inch and the axial length of bushing **232** is about 0.12 inch. Spring **244** is fabricated from a molybdenum chromium nickel cobalt alloy MP35N which is both corrosion resistant and suitable for spring fabrication. The outer diameter of end face **254** of valve element **250** is about 0.027 inch, and the diameter of the circular edge of formation **110** is about 0.027 inch. The outer diameter of shaft section **238** is about 0.168 inch.

The surfaces which guide the longitudinal movement of armature **200** are the pole button weld ring **220** and the annular flange **238**. Flange **238** is provided with four flats at 90 degree intervals around the circumference thereof, two of which are designated and **262 260** in FIG. 2, to allow passage of the fluid flow past flange **238**. Ports **18** and **20** are provided with filters **264** and **268**, respectively, to protect against leaks caused by foreign particles which might otherwise enter valve **10**. Filters **264**, **268** preferably are of the etched titanium type.

In operation, port **18** is connected to an appropriate location in the relatively lower pressure portion of a fluid circuit, and port **20** is connected to a location in the higher pressure portion of the circuit. The armature **200** is moved through the forward stroke in response to electrical energization of the electromagnet **130**. One way of energizing magnet **130** is to charge a capacitor from a battery and then discharge that capacitor through coil **134**. Other procedures can of course be employed for electrically energizing coil **134** in a known manner. Prior to electrical energization of magnet **130**, armature **200** is in the rest position of FIG. 2 where the valve body **250** at the end of armature **200** is firmly seated against the valve seat formation **110** to block fluid communication between port **18** and chamber **14**. The end face **254** of body **250** is held firmly and sealingly against the edge of formation **110** by the force of biasing spring **244**. In the rest position of armature **200**, the pole face of portion **204** is spaced from barrier plate **160** as shown in FIG. 2 thereby defining the gap in the magnetic circuit. In the rest position this gap between the pole face and diaphragm **160** is of maximum length.

When coil **134** is energized, the armature pole portion **240** is attracted toward electromagnet **130** thereby causing armature **200** to be pulled toward diaphragm **160**. Electromagnetic flux travels through the magnetic circuit including core **132**, washer **140**, magnet housing **136**, weld ring **162**, the included portion of the periphery of diaphragm **160** between weld rings **162** and **60**, weld ring **60**, armature pole body **206**, and the gap between the armature pole face and diaphragm **160**. As armature **200** is moved in the forward stroke, i.e. in a direct to the left as viewed in FIG. 2, the armature pole portion **204** moves further into chamber **16**, the armature pole face moves closer to diaphragm **160** thereby decreasing the gap in the magnetic circuit, and the end face **254** of valve element **250** becomes unseated from the annular valve seat formation **110** thereby placing port **18**, chambers **14**, **16** and port **20** in fluid communication. Fluid thus flows from the relatively higher pressure port **20** through chamber **74** and through passages **72** and **70** into chamber **16**, from chamber **16** through passage **90** and recess **92** into chamber **14** and from chamber **14** out through port **18**. The forward stroke of armature **200** is against the biasing force of spring **244** and is completed when the pole face thereof approaches

contact with diaphragm **160**. During the foregoing mode of operation, movement of armature **200** is guided by flange **238** and weld ring **220** relative to the corresponding inner surface portions of the valve housing.

When electrical excitation of coil **134** ceases, armature **200** is moved in the opposite direction, i.e. to the right as viewed in FIG. **2**, by the force of biasing spring **244** until the armature reaches the rest position as shown in FIG. **2** with end face **254** of valve element **250** firmly seated on formation **110**. Armature **200** then remains in the rest position of FIG. **2** closing port **18** and waiting for the next forward stroke which occurs when magnet **130** is energized again. In the illustrative mode where the coil **134** is excited by the discharge of a capacitor therethrough, the time during which valve **10** places ports **18** and **20** in communication, i.e. the time during which valve **10** is open, is relatively short. However, having the valve open for such a relatively short time is called for in typical implantable drug dosage delivery systems. Alternatively, valve **10** can be held open for whatever longer duration may be desired simply by continuing the energization of magnet **130**. In the foregoing mode of operation, when armature **200** initially begins movement toward the rest position for closure of valve **10**, the passage means or channels **176** in barrier **160** serve to shorten the time required for the armature pole **204** to separate from barrier **160** at the outset of armature movement. The passage means or channels **176** also serve to reduce the possibility that the effects of surface tension, if some air should be present within the valve, might cause valve **10** to remain open after electromagnet **130** is no longer energized. In addition, as shown in FIG. **2**, the central portion of barrier **160** radially inwardly of annular groove **170** is provided with a slightly conical shape with the apex or tip of the cone pointing toward or facing armature **200**. The cone thus defined is very blunt and nearly flat, the angle of the cone measured relative to the longitudinal axis of valve **10** being approximately 89°. The taper of this conical central portion of barrier **160** is sufficient to change the behavior of the armature **200** during closing of valve **10** as compared to a completely flat or planar central portion of barrier **160**. In particular, the conical central portion of barrier **160** is believed to prevent the formation of a gas-liquid interface encircling the armature pole face surface **210** in contact with barrier plate **160** which gas-liquid interface could support a pressure difference at the armature pole face sufficient to overcome the force of armature return spring thereby slowing or interfering with closing of valve **10**.

The non-movable diaphragm **160** of titanium or like material provides an hermetic seal between the fluid in housing **12** and the electrical components associated with electromagnet **130**. Having armature **200** immersed in the fluid makes operation of the valve nearly independent of ambient pressure. The initial condition of the valve **10** when armature **200** is in the rest position of FIG. **2** is that fluid is at substantially the same pressure on opposite sides of the armature pole portion **204**, i.e. in the two chambers **14** and **16**.

The valve **10** of the present invention is made electrically and magnetically efficient by minimizing the total gap within the magnetic circuit, by having the magnetic pole face of armature pole portion **204** of relatively large surface area, and by having core **132** of relatively small cross-sectional area. In particular, there is a relatively large contact area at the interface between the axial end face of weld ring **162** and diaphragm **160** and between diaphragm **160** and the axial end face of weld ring **60** to minimize the effective air gap introduced by diaphragm **160** at this point in the magnetic circuit. In other words, diaphragm **160** is relatively thin in relation to the afore-mentioned contact area. Related to this is the need for welding diaphragm **160** to rings **60** and **162** to achieve an hermetic seal between electromagnet **130** and the fluid containing region of housing **12** while at the same time not adversely affecting the magnetic circuit. In addition, there is a relatively large surface area in relation to the gap or space between weld ring **60** and the periphery of armature pole portion **204** to minimize the effective air gap introduced at this point in the magnetic circuit. The relatively small diameter of core **132** provides the necessary number of ampere turns with a minimum electrical resistance. The large area of the pole face of the disc-shaped armature pole portion **204** provides a high magnetic force with a minimum number of ampere turns. Having the magnetic gap external to coil **134**, i.e. between the armature pole face and diaphragm **160**, allows the foregoing features to be achieved simultaneously.

The valve **10** of the present invention is small in size having an overall outer dimension of about 0.31 inch and an over-all length of about 0.96 inch, and has the relatively light weight of about 5.2 grams. A valve of the present invention as described hereinabove can be opened with an initial power drain of as little as 70 milliwatts and held open with 20 milliwatts power drain thereby operating at exceptionally low power levels.

FIGS. **4** and **5** show a valve **300** according to another embodiment of the present invention. Components of valve **300** similar to those of valve **10** are identified by the same reference numeral with a prime designation. A principal difference between the two embodiments is that armature **302** in valve **300** is simpler in structure and relatively easier to manufacture and assemble. In particular armature **302** has a pole portion **304** comprising a solid, monolithic body having the shape or form of a disc. The circumferential surface **306** of pole portion **304** is located relatively close to the inner surface of weld ring **60'** so that armature pole portion **304** occupies a major portion of the volume of chamber **16'**. The lateral dimension of pole portion **304** is several times the longitudinal dimension thereof. Pole portion **304** has a first axial end face **308** which faces toward barrier means **160'** and a second, opposite axial end face **310** which faces toward port **18'**. Thus, end faces **308,310** are disposed substantially perpendicular to the direction of travel of armature **302**.

Pole portion **304** is exclusively of magnetic material, preferably a chrome-molybdenum-iron alloy which is heat treated. Examples are **29-4** and **29-4C** chrome-molybdenum iron alloy. This alloy has high corrosion resistance, and has adequate magnetic characteristics for use in valve **300** when heat treated. In other words, the alloy is heat treated to provide a BH characteristic for the alloy which yields the requisite level of magnetic flux density and coercive force. Furthermore, the alloy is sufficiently resistant to corrosive effects of insulin stabilized for use in implantable drug delivery systems as well as other corrosive drugs.

In particular, the afore-mentioned chrome-molybdenum-iron alloy is a ferritic stainless steel alloy containing 29% chromium, 4% molybdenum and the remainder substantially iron. The afore-mentioned heat treatment involves an anneal and rapid cool of the armature pole portions **302**. In particular the procedure in-

volves a short magnetic anneal at a temperature above that which can form a harmful second phase in the alloy followed by cooling rapidly enough to avoid second phase formation but not so rapidly as to degrade magnetic properties. Heating of armature pole buttons **302** of **29-4** alloy is performed for example in a clamshell furnace at a temperature of about 1010° C. for about twenty minutes whereupon the parts **302** are removed quickly to the ambient in a manner allowing complete cooling for a minimum of 25 minutes. The cooling rate during the first portion of the cooling cycle from 1010° C. down to black, i.e. down to 600° C., should be maintained at about 60 seconds.

The armature body **304** is provided with at least one passage means therethrough, and in the valve shown two axially extending through bores or passages **312,314** are shown. The passages **312,314** extend through the entire axial length of armature body **304** between the axial end faces **308,310**. Passage means **312,314** serve to reduce the time required for armature pole portion **304** to separate from barrier means **160'** during movement of armature **302** toward port **18'** and to reduce surface tension effects between barrier means **106'** and pole portion **304**. The path for fluid flow defined by passage means **312,314** provides the foregoing results when energization of electromagnet **130'** ceases and the force of spring **244'** begins to move armature pole portion **304** away from barrier means **106'**. In addition, barrier **160'** is provided with a central conical formation identical to that of barrier **160** in the embodiment of FIG. **2** and which functions in an identical manner for the same purpose.

Thus, the one-piece pole portion **304** of armature **302** contributes to the simplicity in structure and ease of manufacture and assembly. These advantages also result from the provision of an armature shaft portion **320** which simply is fastened at one end to the pole portion **304**. In particular, armature shaft portion **320** includes a rod-like body **322** having an axial end face **324** which buts the axial end face **310** of pole portion **304**. A rivet **326** or similar fastening means is employed to simply attach shaft portion **320** to pole portion **304**. The outer diameter of rod **322** is slightly smaller than the inner diameter of spring retainer **40'**. As in the previous embodiment, rod **322** is provided with an enlargement at the opposite end which includes two relatively larger diameter sections. In particular, there is a first section **330** which faces pole portion **304** and a second, axially adjacent section **332** which is of larger diameter, the two sections being of relatively short axial length and defining a shoulder therebetween facing pole portion **304** for receiving one end of biasing spring **244'**. As in the previous embodiment, section **332** serves as a guiding flange to provide one of she surfaces which guides the longitudinal movement of armature **300**. Flange **332** is provided with four flats **334** at 90 degree intervals around the circumference thereof, as shown in FIG. **5**, to allow passage of the fluid past flange **332**. The other armature guiding surface is the peripheral surface **306** of armature pole portion **304**.

Armature **302** has a valve portion at the axial end thereof opposite pole portion **304** which valve portion is identical to valve element **250'** of the previous embodiment. In this embodiment, the valve seat formation which is sealingly contacted by end face **254'** of valve element **250'** is defined by the annular edge or junction between the central opening or passage **340** and the conical end face **342** of ferrule element **344** which closes the one axial end of housing **12'**, i.e. the right-hand end as viewed in FIG. **4**. In particular, conical end face **342** is formed on the end of a central body portion **346** of ferrule **344** which fits snugly in the housing inner surface **36'**. Ferrule **344** has an annular body portion **348** which has an inner axial end face **350** which meets the axial end portion **32'** of housing **36'** and an outer axial end face **352**. The outer diameter of body portion **348** is substantially equal to the outer diameter of housing **30'** so that the respective outer surfaces are substantially flush. The conical surface **342** is of simple constructions yet provides an effective valve seat formation. Plunger stroke adjustment is provided by shims **360** which are placed between housing end portion **32'** and end face **350** of ferrule **344**.

By way of example, in an illustrative valve, pole portion **304** has an outer diameter of about 0.264 inch and an axial length of about 0.036 inch, passages **312,314** each have a diameter of about 0.040 inch, rod **322** has an axial length of about 0.16 inch and a diameter of about 0.07 inch, conical surface **342** defines an angle of about 10 degrees with a plane perpendicular to the longitudinal axis of armature **300** and passage **340** has a diameter of about 0.015 inch.

It is therefore apparent that the present invention accomplishes its intended objects. While embodiments of the present invention have been described in detail, that is for the purpose of illustration, not limitation.

What is claimed is:

1. A low power electromagnetic valve for use with implantable fluid delivery systems, said valve comprising:

a) a housing including a fluid containing region having first and second chambers and first and second ports in fluid communication with said first and second chambers, respectively;

b) electromagnet means carried by said housing and located externally of said fluid containing region;

c) barrier means of fluid-impervious material for isolating said electromagnet means from said fluid containing region of said housing;

d) an armature movably positioned in said fluid containing region of said housing and having a pole portion located in one of said first and second chambers for magnetic attraction by said electromagnet means and having a plunger portion provided with valve means located in the other of said first and second chambers for opening and closing one of said ports to place said ports in fluid communication through said fluid containing region of said housing in one control state of said valve and to block fluid communication between said ports through said fluid containing region of said housing in another control state of said valve;

e) said armature pole portion comprising a solid body exclusively of corrosion resistent magnetic material occupying a major portion of the one of said chambers in which it is located and having a lateral dimensions several times greater than the longitudinal dimensions thereof, said magnetic material consisting essentially of a heat treated alloy of chrome, molybdenum and iron; and

f) means for defining a magnetic circuit including said electromagnet, said armature pole portion, a portion of said barrier means and a gap between said pole portion and said electromagnet means located in said fluid containing region of said housing and external to said electromagnet means for closing

said gap in response to electrical energization of said electromagnet to move said armature and change the control state of said valve.

2. A valve according to claim 1, wherein said armature pole portion contacts a surface of said barrier means when said gap is closed to change the control state of said valve and wherein said pole portion is provided with passage means through the body thereof to reduce the time required for said pole portion to separate from said barrier means during movement of said armature and to reduce surface tension effects between said barrier means and said pole portion.

3. A valve according to claim 1, wherein said armature pole portion and said plunger portion are of fixed length and wherein said one port is located in a component of said housing separated from the remainder of said housing by shim means so as to allow adjustment of the distance between said one port and said valve means on said plunger portion.

4. A valve according to claim 1, wherein said valve means comprises a valve seat carried by said plunger and having a surface disposed substantially perpendicular to the direction of travel of said armature and wherein said one port is defined on an inner surface of said housing having a frusto conical formation diverging away from said valve seat surface to facilitate initial fluid flow upon opening of said valve.

5. A valve according to claim 1, wherein said armature plunger portion is provided with guiding means in the form of a flange disposed substantially perpendicular to the direction of armature travel and having a peripheral surface in closely spaced relation to the inner surface of said housing.

6. A valve according to claim 5, further including at least one flow passage means formed in said peripheral surface of said flange.

7. A valve according to claim 1, wherein said housing is elongated having a longitudinal axis, said armature being positioned for movement along said housing longitudinal axis, and wherein said fluid containing region of said housing and said electromagnet means are in axially spaced relation along said housing longitudinal axis.

8. A valve according to claim 1, wherein said armature pole portion is formed of an alloy of chrome, molybdenum and iron and then subjected to magnetic annealing for a relatively short time at a temperature above that which can form a harmful second phase in the alloy followed by cooling at a rate rapid enough to avoid second phase formation but not so rapid as to degrade the magnetic properties of the alloy.

9. A low power electromagnetic valve for use with implantable fluid delivery systems, said valve comprising:

a) a housing including a fluid containing region having first and second chambers and first and second pores in fluid communication with said first and second chambers, respectively;

b) electromagnet means carried by said housing and located externally of said fluid containing region;

c) barrier means of fluid-impervious material for isolating said electromagnet means from said fluid containing region of said housing;

d) an armature movably positioned in said fluid containing region of said housing and having a pole portion located in one of said first and second chambers for magnetic attraction by said electromagnet means and having a plunger portion provided with valve means located in the other of said first and second chambers for opening and closing one of said ports to place said ports in fluid communication through said fluid containing region of said housing in one control state of said valve and to block fluid communication between said ports through said fluid containing region of said housing in another control state of said valve;

e) said housing being elongated having a longitudinal axis, said armature being positioned for movement along said housing longitudinal axis, and said fluid containing region of said housing and said electromagnet means being in axially spaced relation along said housing longitudinal axis;

f) said armature pole portion occupying a major portion of the one of said chambers in which it is located and having a lateral dimension several times greater than the longitudinal dimension thereof;

g) said armature pole portion having a fluid-containing section of material which is compatible with the fluid delivered by said system;

h) means for defining a magnetic circuit including said electromagnet, said armature pole portion, a portion of said barrier means and a gap between said pole portion and said electromagnet means located in said fluid containing region of said housing and external to said electromagnet means for closing said gap in response to electrical energization of said electromagnet to move said armature and change the control state of said valve; and

i) said armature pole portion contacting said barrier means when said gap is closed to change the control state of said valve and said barrier means including a surface portion of conical shape wherein the apex of the cone faces toward said armature pole portion so as to enhance the separation of said pole portion from said barrier means during movement of said armature.

10. A low power electromagnetic valve for use with implantable fluid delivery systems, said valve comprising:

a) a housing including a fluid containing region having first and second chambers and first and second ports in fluid communication with said first and second chambers, respectively;

b) electromagnet means carried by said housing and located externally of said fluid containing region;

c) barrier means of fluid-impervious material for isolating said electromagnet means from said fluid containing region of said housing;

d) an armature movably positioned in said fluid containing region of said housing and having a pole portion located in one of said first and second chambers for magnetic attraction by said electromagnet means and having a plunger portion provided with valve means located in the other of said first and second chambers for opening and closing one of said ports to place said ports in fluid communication through said fluid containing region of said housing in one control state of said valve and to block fluid communication between said ports through said fluid containing region of said housing in another control state of said valve;

e) said armature pole portion comprising a solid body exclusively of magnetic material occupying a major portion of the one of said chambers in which it is located and having a lateral dimension several times greater than the longitudinal dimensions

thereof, said magnetic material consisting essential of a heat treated alloy of chrome, molybdenum and iron;

f) means for defining a magnetic circuit including said electromagnet, said armature pole portion, a portion of said barrier means and a gap between said pole portion of said electromagnet means located in said fluid containing region of said housing and external to said electromagnet means for closing said gap in response to electrical energization of said electromagnet to move said armature and change the control state of said valve; and

g) said armature pole portion contacting said barrier means when said gap is closed to change the control state of said valve and said barrier means including a surface portion of conical shape wherein the apex of the cone faces toward said armature pole portion so as to enhance the separation of said pole portion from said barrier means during movement of said armature.

11. A low power electromagnetic valve for use with implantable fluid delivery systems, said valve comprising:

a) a housing including a fluid containing region having first and second chambers and first and second ports in fluid communication with said first and second chambers, respectively;

b) electromagnet means carried by said housing and located externally of said fluid containing region;

c) barrier means of fluid-impervious material for isolating said electromagnet means from said fluid containing region of said housing;

d) an armature movably positioned in said fluid containing region of said housing and having a pole portion located in one of said first and second chambers for magnetic attraction by said electromagnet means and having a plunger portion provided with valve means located in the other of said first and second chambers for opening and closing one of said ports no place said ports in fluid communication through said fluid containing region of said housing in one control state of said valve and to block fluid communication between said ports through said fluid containing region of said housing in another control state of said valve;

e) said housing being elongated having a longitudinal axis, said armature being positioned for movement along said housing longitudinal axis, and said fluid containing region of said housing and said electromagnet means being in axially spaced relation along said housing longitudinal axis;

f) said armature pole portion occupying a major portion of the one of said chambers in which it is located and having a lateral dimension several times greater than the longitudinal dimension thereof;

g) said armature pole portion having a fluid-contacting section of material which is compatible with and corrosion resistant to the fluid delivered by said system, said armature pole portion comprising a body of magnetic material within a titanium enclosure; and

h) means for defining a magnetic circuit including said electromagnet, said armature pole portion, a portion of said barrier means and a gap between said pole portion and said electromagnet means located in said fluid containing region of said housing and external to said electromagnet means for closing said gap in response to electrical energization of said electromagnet to move said armature and change the control state of said valve.

12. A valve according to claim **11**, wherein said body is in the form of a disc and wherein said enclosure comprises a cap having a base contacting one axial face of said disc and an annular rim contacting the periphery of said disc and a disc-shaped body contacting the opposite axial end face of said disc and abutting said rim of said cap.

13. A valve according to claim **12**, wherein said rim of said cap extends slightly axially beyond the periphery of said disc and said disc-shaped body fits within and contacts said rim of said cap and further including a weld ring embracing the periphery of said rim so that said ring, rim and disc-shaped body can be welded together at the junctions thereof.

14. A valve according to claim **12**, further including at least one vent passage provided in said disc shaped body to evacuate residual gas during assembly, said passage being sealed by a plug after assembly.

15. A valve according to claim **11**, wherein said body is of nickel-iron alloy.

16. A valve according to claim **11**, wherein said armature pole portion is in the shape of a disc wherein the opposite axial end faces of said disc are disposed substantially perpendicular to the direction of travel of said armature and wherein the periphery of said disc is located close to the inner surface of said housing.

17. A valve according to claim **11**, further including filter means at said first and second ports.

18. A valve according to claim **11**, wherein said valve means comprises a valve element associated with said one port and a valve seat carried by said plunger for contacting said valve element.

19. A valve according to claim **18**, wherein said valve element comprises an annular body surrounding said one port and provided with a sharp annular edge axially facing toward said valve seat, and wherein said valve seat comprises a body of elastomer material on the end of said plunger having a flat axial surface adapted to sealingly contact said annular edge.

20. A valve according to claim **11**, wherein said valve means comprises a valve seat carried by said plunger and having a surface disposed substantially perpendicular to the direction of travel of said armature and wherein said one port is defined on an inner surface of said housing having a frusto conical formation diverging away from said valve seat surface to facilitate initial fluid flow upon opening of said valve.

21. A low power electromagnetic valve for use with implantable fluid delivery systems, said valve comprising:

a) a housing including a fluid containing region having first and second chambers and first and second ports in fluid communication with said first and second chambers, respectively;

b) electromagnet means carried by said housing and located externally of said fluid containing region;

c) barrier means of fluid-impervious material for isolating said electromagnet means from said fluid containing region of said housing;

d) an armature movably positioned in said fluid containing region of said housing and having a pole portion located in one of said first and second chambers for magnetic attraction by said electromagnet means and having a plunger portion provided with valve means located in the other of said first and second chambers for opening and closing

one of said ports to place said ports in fluid communication through said fluid containing region of said housing in one control state of said valve and to block fluid communication between said ports through said fluid containing region of said housing in another control state of said valve;

e) said housing being elongated having a longitudinal axis, said armature being positioned for movement along said housing longitudinal axis, and said fluid containing region of said housing and said electromagnet means being in axially spaced relation along said housing longitudinal axis;

f) said armature pole portion occupying a major portion of the one of said chambers in which it is located and having a lateral dimension several times greater than the longitudinal dimension thereof;

g) said armature pole portion having a fluid-contacting section of material which is compatible with and corrosion resistant to the fluid delivered by said system; and

h) means for defining a magnetic circuit including said electromagnet, said armature pole portion, a portion of said barrier means and a gap between said pole portion and said electromagnet means located in said fluid containing region of said housing and external to said electromagnet means for closing said gap in response to electrical energization of said electromagnet to move said armature and change the control state of said valve;

i) said armature pole portion contacting a surface of said barrier means when said gap is closed to change the control state of said valve and said barrier means being provided with passage means along said surface to reduce the time required for said pole portion to separate from said barrier means during movement of said armature and to reduce surface tension effects between said barrier and said pole portion.

22. A valve according to claim 21, wherein said armature pole portion has a peripheral surface in closely spaced relation to the inner surface of said housing and further including longitudinally extending passage means formed in said peripheral surface for co-operating with said passage means on said barrier means.

23. A valve according to claim 21, wherein said armature pole portion has a peripheral surface in closely spaced relation to the inner surface of said housing and further including longitudinally extending passage means formed in said housing inner surface adjacent said pole portion peripheral surface for co-operating with said passage means on said barrier means.

24. A low power electromagnetic valve for use with implantable fluid delivery systems, said valve comprising:

a) a housing including a fluid containing region having first and second chambers and first and second pores in fluid communication with said first and second chambers, respectively;

b) electromagnet means carried by said housing and located externally of said fluid containing region;

c) barrier means of fluid-impervious material for isolating said electromagnet means from said fluid containing region of said housing;

d) an armature movably positioned in said fluid containing region of said housing and having a pole portion located in one of said first and second chambers for magnetic attraction by said electromagnet means and having a plunger portion provided with valve means located in the other of said first and second chambers for opening and closing one of said ports to place said ports in fluid communication through said fluid containing region of said housing in one control state of said valve and to block fluid communication between said ports through said fluid containing region of said housing in another control state of said valve;

e) said armature pole portion being provided with a longitudinally extending bushing and said armature plunger portion comprising a shaft received in said bushing so that the length of the plunger can be changed to adjust the stroke;

f) said housing being elongated having a longitudinal axis, said armature being positioned for movement along said housing longitudinal axis, and said fluid containing region of said housing and said electromagnet means being in axially spaced relation along said housing longitudinal axis;

g) said armature pole portion occupying a major portion of the one of said chambers in which it is located and having a lateral dimension several times greater than the longitudinal dimension thereof;

h) said armature pole portion having a fluid-contacting section of material which is compatible with and corrosion resistant to the fluid delivered by said system; and

i) means for defining a magnetic circuit including said electromagnet, said armature pole portion; a portion of said barrier means and a gap between said pole portion and said electromagnet means located in said fluid containing region of said housing and external to said electromagnet means for closing said gap in response to electrical energization of said electromagnet to move said armature and change the control state of said valve.

25. A low power electromagnetic valve for use with implantable fluid delivery systems, said valve comprising:

a) a housing including a fluid containing region having first and second chambers and first and second ports in fluid communication with said first and second chambers, respectively;

b) electromagnet means carried by said housing and located externally of said fluid containing region;

c) barrier means of fluid-impervious material for isolating said electromagnet means from said fluid containing region of said housing;

d) an armature movably positioned in said fluid containing region of said housing and having a pole portion located in one of said first and second chambers for magnetic attraction by said electromagnet means and having a plunger portion provided with valve means located in the other of said first and second chambers for opening and closing one of said ports to place said ports in fluid communication through said fluid containing region of said housing in one control state of said valve and to block fluid communication between said ports through said fluid containing region of said housing in another control state of said valve;

e) said housing being elongated having a longitudinal axis, said armature being positioned for movement along said housing longitudinal axis, and said fluid containing region of said housing and said electromagnet means being in axially spaced relation along said housing longitudinal axis;

f) said armature pole portion occupying a major portion of the one of said chambers in which it is located and having a lateral dimension several times greater than the longitudinal dimension thereof;

g) said armature pole portion having a fluid-contacting section of material which is compatible with and corrosion resistant to the fluid delivered by said system;

h) means for defining a magnetic circuit including said electromagnet, said armature pole portion, a portion of said barrier means and a gap between said pole portion and said electromagnet means located in said fluid containing region of said housing and external to said electromagnet means for closing said gap in response to electrical energization of said electromagnet to move said armature and change the control state of said valve; and

i) said armature plunger portion being provided with guiding means in the form of a flange disposed substantially perpendicular to the direction of armature travel and having a peripheral surface in closely spaced relation to the inner surface of said housing.

26. A valve according to claim 25, further including at least one flow passage means formed in said peripheral surface of said flange.

27. A low power electromagnetic valve for use with implantable fluid delivery systems, said valve comprising:

a) a housing including a fluid containing region having first and second chambers and first and second ports in fluid communication with said first and second chambers, respectively;

b) electromagnet means carried by said housing and located externally of said fluid containing region;

c) barrier means of fluid-impervious material for isolating said electromagnet means from said fluid containing region of said housing;

d) an armature movably positioned in said fluid containing region of said housing and having a pole portion located in one of said first and second chambers for magnetic attraction by said electromagnet means and having a plunger portion provided with valve means located in the other of said first and second chambers for opening and closing one of said ports to place said ports in fluid communication through said fluid containing region of said housing in one control state of said valve and to block fluid communication between said ports through said fluid containing region of said housing in another control state of said valve;

e) said housing being elongated having a longitudinal axis, said armature being positioned for movement along said housing longitudinal axis, and said fluid containing region of said housing and said electromagnet means being in axially spaced relation along said housing longitudinal axis;

f) said armature pole portion occupying a major portion of the one of said chambers in which it is located and having a lateral dimension several times greater than the longitudinal dimension thereof;

g) said armature pole portion having a fluid-contacting section of material which is compatible with and corrosion resistant to the fluid delivered by said system, said armature pole portion comprising a solid body of chrome-molybdenum-iron alloy heat treated to provide enhanced magnetic flux density and coercive force properties; and

h) means for defining a magnetic circuit including said electromagnet, said armature pole portion, a portion of said barrier means and a gap between said pole portion and said electromagnet means located in said fluid containing region of said housing and external to said electromagnet means for closing said gap in response no electrical energization of said electromagnet to move said armature and change the control state of said valve.

28. A low power electromagnetic valve for use with implantable fluid delivery systems, said valve comprising:

a) a housing including a fluid containing region having first and second chambers and first and second ports in fluid communication with said first and second chambers, respectively;

b) electromagnet means carried by said housing and located externally of said fluid containing region;

c) barrier means of fluid-impervious material for isolating said electromagnet means from said fluid containing region of said housing;

d) an armature movably positioned in said fluid containing region of said housing and having a pole portion located in one of said first and second chambers for magnetic attraction by said electromagnet means and having a plunger portion provided with valve means located in the other of said first and second chambers for opening and closing one of said ports to place said ports in fluid communication through said fluid containing region of said housing in one control state of said valve and to block fluid communication between said ports through said fluid containing region of said housing in another control state of said valve;

e) said armature pole portion and said plunger portion being of fixed length and said one port being located in a component of said housing separated from the remainder of said housing by shim means so as to allow adjustment of the distance between said one port and said valve means on said plunger portion;

f) said housing being elongated having a longitudinal axis, said armature being positioned for movement along said housing longitudinal axis, and said fluid containing region of said housing and said electromagnet means being in axially spaced relation along said housing longitudinal axis;

g) said armature pole portion occupying a major portion of the one of said chambers in which it is located and having a lateral dimension several times greater than the longitudinal dimension thereof;

h) said armature pole portion having a fluid-contacting section of material which is compatible with and corrosion resistant to the fluid delivered by said system; and

i) means for defining a magnetic circuit including said electromagnets said armature pole portion, a portion of said barrier means and a gap between said pole portion and said electromagnet means located in said fluid containing region of said housing and external to said electromagnet means for closing said gap in response to electrical energization of said electromagnet to move said armature and change the control state of said valve.

* * * * *

EXHIBIT D

Copy of the Maintenance Fee Receipts and Copy of the Certificate of Correction

Commissioner for Patents
United States Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450
www.uspto.gov

Customer No 76656 | ISTMT | DATE PRINTED 08/22/2012

Patent Docket Department
Armstrong Teasdale LLP
7700 Forsyth Boulevard
Suite 1800
St. Louis MO 63105

MAINTENANCE FEE STATEMENT

According to the records of the U.S. Patent and Trademark Office (USPTO), the maintenance fee and any necessary surcharge have been timely paid for the patent listed below. The "PYMT DATE" column indicates the payment date (i.e., the date the payment was filed).

The payment shown below is subject to actual collection. If the payment is refused or charged back by a financial institution, the payment will be void and the maintenance fee and any necessary surcharge unpaid.

Direct any questions about this statement to: Mail Stop M Correspondence, Director of the USPTO, P.O.Box 1450, Alexandria, VA 22313-1450.

PATENT NUMBER	FEE AMT	SUR CHARGE	PYMT DATE	U.S. APPLICATION NUMBER	PATENT ISSUE DATE	APPL. FILING DATE	PAYMENT YEAR	SMALL ENTITY?	ATTY DKT NUMBER
5,368,274	**$1,050.00**	**$0.00**	**03/09/98**	**07/946,392**	**11/29/94**	**09/17/92**	**04**	**NO**	

Commissioner for Patents
United States Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450
www.uspto.gov

Customer No 76656 | ISTMT | DATE PRINTED 08/22/2012

Patent Docket Department
Armstrong Teasdale LLP
7700 Forsyth Boulevard
Suite 1800
St. Louis MO 63105

MAINTENANCE FEE STATEMENT

According to the records of the U.S.Patent and Trademark Office (USPTO), the maintenance fee and any necessary surcharge have been timely paid for the patent listed below. The "PYMT DATE" column indicates the payment date (i.e., the date the payment was filed).

The payment shown below is subject to actual collection. If the payment is refused or charged back by a financial institution, the payment will be void and the maintenance fee and any necessary surcharge unpaid.

Direct any questions about this statement to: Mail Stop M Correspondence, Director of the USPTO, P.O.Box 1450, Alexandria, VA 22313-1450.

PATENT NUMBER	FEE AMT	SUR CHARGE	PYMT DATE	U.S. APPLICATION NUMBER	PATENT ISSUE DATE	APPL. FILING DATE	PAYMENT YEAR	SMALL ENTITY?	ATTY DKT NUMBER
5,368,274	**$1,010.00**	**$0.00**	**05/21/02**	**07/946,392**	**11/29/94**	**09/17/92**	**08**	**NO**	

Commissioner for Patents
United States Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450
www.uspto.gov

Customer No 76656 | ISTMT | DATE PRINTED 08/22/2012

Patent Docket Department
Armstrong Teasdale LLP
7700 Forsyth Boulevard
Suite 1800
St. Louis MO 63105

MAINTENANCE FEE STATEMENT

According to the records of the U.S.Patent and Trademark Office (USPTO), the maintenance fee and any necessary surcharge have been timely paid for the patent listed below. The "PYMT DATE" column indicates the payment date (i.e., the date the payment was filed).

The payment shown below is subject to actual collection. If the payment is refused or charged back by a financial institution, the payment will be void and the maintenance fee and any necessary surcharge unpaid.

Direct any questions about this statement to: Mail Stop M Correspondence, Director of the USPTO, P.O.Box 1450, Alexandria, VA 22313-1450.

PATENT NUMBER	FEE AMT	SUR CHARGE	PYMT DATE	U.S. APPLICATION NUMBER	PATENT ISSUE DATE	APPL. FILING DATE	PAYMENT YEAR	SMALL ENTITY?	ATTY DKT NUMBER
5,368,274	**$3,800.00**	**$0.00**	**05/24/06**	**07/946,392**	**11/29/94**	**09/17/92**	**12**	**NO**	

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 5,368,274

DATED : November 29, 1994

INVENTOR(S) : Theodore J. Falk, Richard Brown, Lawrence E. Morris, Norbert W. Franz, Jr.

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Title page, item [75],
Change the name of the Inventor from"Franz" to --Frenz--.

Signed and Sealed this

Eighteenth Day of April, 1995

Bruce Lehman

BRUCE LEHMAN

Commissioner of Patents and Trademarks

Attest:

Attesting Officer

EXHIBIT E

Demonstration of Independent Claim 1

EXHIBIT E

Descriptions of the Prometra® Programmable Pump System and the valve system used in that system are taken from the documents comprising Exhibit A unless otherwise noted. The following table compares the elements of claim 1 of the Valve Patent to the valve system.

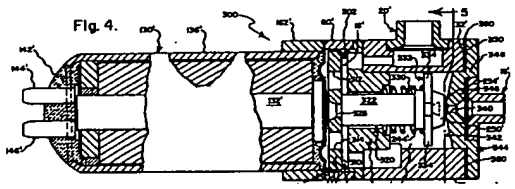
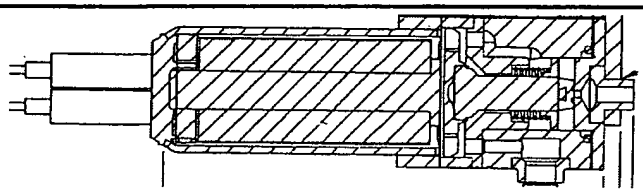
 **Fig. 4 from the Valve Patent**	 **From Fig. 1 of the V53 Assembly Specification**
1. A low power electromagnetic valve for use with implantable fluid delivery systems, said valve comprising:	The implantable fluid delivery system referenced is the Prometra® Programmable Pump System (the "Medical Device") which is designed to administer a controlled delivery of Infumorph® directly into a user's spinal cord. Patient Guide, 5, 29. The use of the valves patented in U.S. Patent No. 5,368, 274 (the "Valve Patent") in the Medical Device resulted in a drug delivery accuracy of 96.8% with a 90% confidence interval of 95.5%–97.7% during a six-month clinical trial. Patient Guide, 18–19. As demonstrated by Figure 1 in the Patient Guide, page 42, the valve is a fundamental component of the Medical Device. As shown in the diagram of the actual valve used in the V53 Assembly Specification document, page 42, the valve used in the Medical Device is claimed in the Valve Patent. The valve is an incorporated component of the Medical Device, which also includes a Dosing Chamber. The Medical Device is described as having a "triple redundancy flow controller system," which is the device disclosed in the Valve Patent. Patient Guide, 30. That "triple redundancy flow control system," *i.e.* the valve, provides for a precise and accurate flow rate of drugs. Patient Guide, 31. Further, the valves and corresponding Dosing Chamber are "the most mechanically complex component[s] of an implantable pump," and the valves also consume very little energy from the implanted battery, extending the life of the battery. White Paper, 6–7.

EXHIBIT E

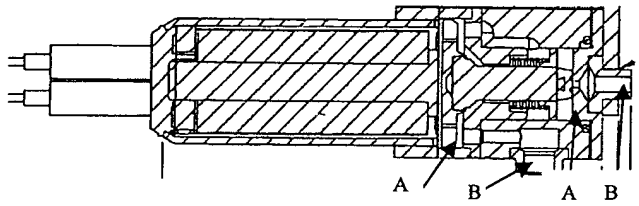
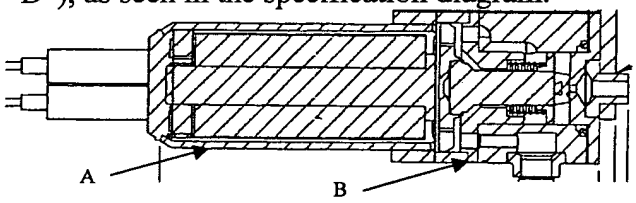
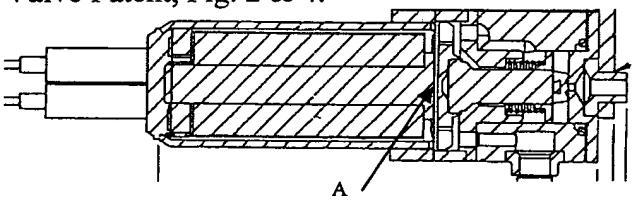
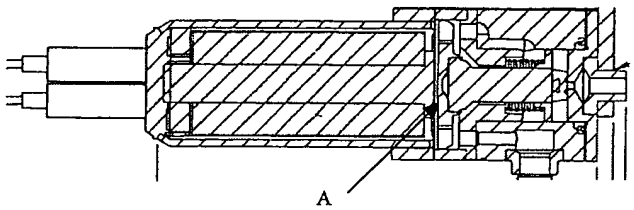
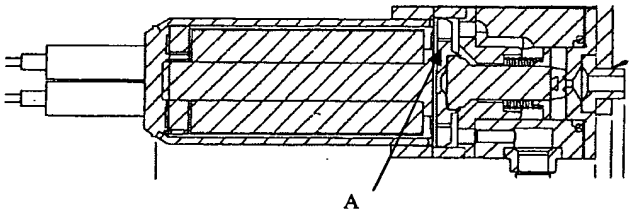
a) a housing including a fluid containing region having first and second chambers and first and second ports in fluid communication with said first and second chambers, respectively;	Two valves are used in the Medical Device, such that there is an "inlet valve" that receives inflowing fluid and there is an "outlet valve" that allows fluid to flow out. White Paper, 5. Each valve has a casing (the housing) allowing fluid to flow into the valve casing (the fluid containing region) from an inlet port and then through the outlet port (first and second ports). White Paper, 5. As shown by the diagram included with the V53 Valve Set Assembly Specifications material, there are two chambers (labeled "A") in respective communication with the inlet and outlet ports (labeled "B"). 
b) electromagnet means carried by said housing and located externally of said fluid containing region;	The valves manufactured to be used with the Medical Device require the electromagnetic coil windings and electrical leads to be insulated from the case and any other rounded parts. V53 Valve Set Assembly Specifications, 8. This insulation necessarily requires the electromagnetic portions of the valve (labeled generally as "A") not to be contained in the fluid-containing region of the housing (labeled generally as "B"), as seen in the specification diagram. 
c) barrier means of fluid-impervious material for isolating said electromagnet means from said fluid containing region of said housing;	The electromagnetic components are part of the valve casing are isolated from the fluid-containing region through barrier material (labeled "A"). V53 Valve Set Assembly Specifications, Attachment 1. *See also*, Valve Patent, Fig. 2 & 4. 

EXHIBIT E

d) an armature movably positioned in said fluid containing region of said housing and having a pole portion located in one of said first and second chambers for magnetic attraction by said electromagnet means and having a plunger portion provided with valve means located in the other of said first and second chambers for opening and closing one of said ports to place said ports in fluid communication through said fluid containing region of said housing in one control state of said valve and to block fluid communication between said ports through said fluid containing region of said housing in another control state of said valve;	The armature plunger (labeled "A") referenced in the claim is illustrated in the assembly specifications.  Using the electromagnetic means attached to the housing of the valve, the valve becomes "open" (thereby placing the inlet and outlet ports in fluid communication) when the electromagnet is energized. V53 Valve Set Assembly Specifications, 3. The valve is closed (thereby blocking the fluid communication between the two ports) by de-energizing the electromagnet and having a spring return the armature to default position. V53 Valve Set Assembly Specifications, 3.
e) said armature pole portion comprising a solid body exclusively of corrosion resistent magnetic material occupying a major portion of the one of said chambers in which it is located and having a lateral dimensions several times greater than the longitudinal dimensions thereof, said magnetic material consisting essentially of a heat treated alloy of chrome, molybdenum and iron; and	The armature pole portion referenced is labeled "A" in the diagram below. As is demonstrated, its lateral dimensions are greater than its longitudinal dimensions, and it occupies a major portion of the chamber in which it resides.  All metals used in fabricating the valve are "corrosion resistant or plated or treated to resist corrosion when dissimilar metals are used in intimate contact with each other." V53 Assembly Specification, 7. *See also* V53 Assembly Specification, Attachment 1, Figure 1 (showing the same or a substantially similar representation of the armature pole portion that responds to energizing of the electromagnetic component of the valve).

f) means for defining a magnetic circuit including said electromagnet, said armature pole portion, a portion of said barrier means and a gap between said pole portion and said electromagnet means located in said fluid containing region of said housing and external to said electromagnet means for closing said gap in response to electrical energization of said electromagnet to move said armature and change the control state of said valve.	As stated above, the valve contains an electronically activated solenoid. Principles of Operation, 1. When the coil in the valve casing is energized, it causes the valve to open. When energy is no longer applied to the coil, a return spring causes the armature to return to the closed position. V53 Assembly Specification, 3. The Medical Device uses a pair of valves such that both valves are never opened at the same time, meaning that both valves are never energized to open simultaneously. White Paper, 5. The valve is energized by a battery encased in the Medical Device. Patient Guide, 19. The life of the battery is dependent on the rate at which the valve allows delivery of the drug, such that a higher flow rate results in a shorter battery life. Patient Guide, 19.

EXHIBIT F

Statement of Relevant Dates and Information Required Under 35 U.S.C. § 156(g)

EXHIBIT F

STATEMENT OF RELEVANT DATES AND INFORMATION REQUIRED UNDER 35 U.S.C. § 156(g) TO DETERMINE THE APPLICABLE REGULATORY REVIEW PERIOD FOR A MEDICAL DEVICE

1) The Effective Date of the Investigational Device Exemption (IDE) and the IDE Number

Applicant submitted IDE # G060192 on September 15, 2006, with the FDA granting conditional approval for the IDE in a letter dated October 19, 2006. Applicant responded to the FDA's questions in the October 19, 2006 letter on December 1, 2006. The FDA fully approved the IDE in a letter issued to Applicant on January 1, 2007.

2) The Date On Which the Application for Product Approval under § 515 of the Federal Food, Drug, and Cosmetic Act Was Initially Submitted & the Application Number

Applicant opted to pursue regulatory approval through the FDA's Premarket Approval Application Modular Review program. Applicant submitted the following:

Submission (FDA Reference No.)	Submission Date
PMA Module 1 (M070007.M001)	August 24, 2007
PMA Module 2 (M070007.M002)	January 31, 2008
PMA Module 3 (M070007.M003)	December 13, 2007
PMA Module 4 (M070007.M004)	April 3, 2008

The FDA had received all modules and filed the PMA submission on April 11, 2008. The application number for the full PMA is P080012.

3) The Date On Which the Application Was Approved

As of the submission of this application for interim patent term extension, the FDA has not given Applicant final approval to use or market the Medical Device commercially. In a letter to Applicant dated February 7, 2012, the FDA approved the PMA with BARD as the manufacturer of several components of the Medical Device: the filter seal, the suture wings, the cannula strain relief, and the guidewire. However, during the pendency of the regulatory review period, BARD ceased production of these components, requiring Applicant to obtain these items from a different manufacturer. While the FDA's February 7, 2012 letter states that Applicant could begin commercial distribution of the Medical Device, the FDA has since withheld final permission to use or market the Medical Device commercially until it determines that the components produced by the new manufacturer (Proven Process Medical Devices, Inc.) are acceptable. Thus, the regulatory review of the Medical Device is continuing, and Applicant is still unable to use or market the Medical Device commercially.

EXHIBIT G

A Brief Description of Significant Activities Undertaken by Applicant During the Regulatory Review Period

EXHIBIT G

A BRIEF DESCRIPTION OF THE SIGNIFICANT ACTIVITIES UNDERTAKEN BY APPLICANT DURING THE APPLICABLE REGULATORY REVIEW PERIOD

The Preliminary Regulatory Review Period (IDE)

Description of Event	Submission/ Event Date	FDA Receipt Date	FDA Letter Issue Date	FDA Response
Submission of Original IDE # G060192	9/15/2006	10/19/2006	10/19/2006	Conditionally Approved
InSet response to questions from FDA letter dated 10/19/06	12/1/2006	12/4/2006	1/3/2007	Fully Approved IDE
InSet submission of minor modifications to protocol	2/5/2007	2/8/2007	3/2/2007	Approved
First Patient Enrolled in IDE Study	3/10/07			
Submission of 2008 Annual Progress Report for PUMP-1	1/25/2008	1/28/2008	2/26/2008	Add'l Info. Required—2008 Annual Progress Report Question Set #1
InSet submission of Six-Month Report	1/25/08	1/28/2008		
Submission of InSet modifications to clinical trial	2/20/08		3/21/2008	Approved
IDE Study stops enrollment of new patients	2/25/08			

Exhibit G

InSet response to 2008 Annual Progress Report Question Set #1	2/29/2008		4/2/2008	Add'l Info. Required—2008 Annual Progress Report Question Set #2
Request for continued access for clinical trial	2/29/2008	3/3/2008	4/2/2008	Disapproved—Continued Access Question Set #1
Final clinical report completed	3/20/08			
InSet response to 2008 Annual Progress Report Question Set #2 (amended on 06/05/08)	5/31/2008		6/27/2008	Add'l Info. Required—2008 Annual Progress Report Question Set #3
InSet resubmission of IDE continued access request, addressing FDA's previous concerns in prior disapproval	5/30/2008		7/2/2008	Disapproved—Continued Access Question Set #2
Submission of addendum to InSet's response to Question Set #2 from FDA's response to the 2008 Annual Progress Report & submission of additional clinical information	6/5/2008		6/27/2008	Add'l Info. Required—2008 Annual Progress Report Question Set #3
InSet submission for compassionate use of Hydromorphone for Patient 10506	6/4/08		6/26/2008	Approved
InSet response to 2008 Annual Progress Report Question Set #3	8/8/2008	8/12/2008		Approved

Exhibit G

InSet submission of revised clinical protocol for Continued Access	9/10/2008		10/9/2008	Conditionally Approved for 2 institutes, 22 subjects—Continued Access Question Set #3
InSet request for compassionate use of Dilaudid for Patient 10121	9/23/08		10/24/2008	Approved
InSet request for compassionate use of Hydromorphone for Patient 10512	11/14/2008	11/17/2008	12/17/2008	Disapproved (recommended IND)
Response to Continued Access Question Set # 3	12/1/2008	12/3/2008	12/30/2008	Conditionally. Approved for 2 institutes, 22 subjects—Continued Access Question Set #4
Response to Continued Access Question Set # 4	1/6/2009	1/6/2009	1/30/2009	Fully Approved for 7 institutes, 90subj
Submission of 2009 Annual Progress Report—PUMP1	1/9/2009	1/12/2009	2/11/2009	Add'l Info. Required—2009 Annual Progress Report Question Set #1
Submission of pump and catheter material updates and sterilization contractor changes (additional Email communication conducted)	2/10/2009	2/11/2009	3/13/2009	Approved
Response to 2009 Annual Progress Report Question Set #1	3/9/2009	3/11/2009	05/12/09	Issued General Letter of Concern

Exhibit G

Response to FDA's General Letter of Concern 05/12/09; proposal to limit new patients enrolled to Infumorph only	5/27/2009	6/2/2009	6/2/2009	Disapproved—scheduled meeting for 7/21/09
Submission for protocol changes using Infumorph	8/10/2009	8/12/2009	9/11/2009	Approved
Submission of Current Investigator Report	9/11/2009	9/25/2009		
Submission of proposal to add 3 sites to PUMP2 study	11/19/2009	11/23/2009	12/18/2009	Disapproved
Submission of 2010 Annual Progress Report for PUMP1 & PUMP2	2/1/2010	2/17/2010	3/19/2010	No Add'l Info Required—Raised concerns and suggested protocol revision
Response to concerns raised from the 2010 Annual Progress Report	7/2/2010	7/6/2010		
Protocol modification (P-01rev6 and P-02rev5) to add mechanism for withdrawn patient follow-up and support	7/20/2010	7/21/2010	8/19/2010	Fully Approved 7 institutes, 90 subjects
InSet submission of Current Investigator Report–2010	8/20/2010	8/23/2010		
Submission of protocol modification (P-01rev8 and P-02rev7) to add additional follow-up data collection to support regulatory submissions	9/13/2010	9/14/2010		

Exhibit G

Pump changed to ceramic crystal, extending the shelf life of catheter from 6 months to 2 years and the shelf life of the pump from 1 year to 2 years	10/25/2010	10/27/2010	11/26/2010	Requested attachments
Submission of Applicant name change from InSet to Medasys (sent on Medasys letterhead)	12/1/2010	12/3/2010		Requested a copy on InSet letterhead
Submission of Applicant name change from InSet to Medasys (sent on InSet letterhead)	12/7/2010	12/8/2010		
Response to question from FDA's conditional approval letter dated 11/26/10, regarding the pump change to ceramic crystal, extending the shelf life of catheter from 6 months to 2 years and extending the shelf life of the pump from 1 year to 2 years	1/7/2011	1/10/2011	2/9/2011	Conditionally approved—Pump Change Question Set
Submission of Final Report for PUMP-1	2/15/2011	2/16/2011	3/15/2011	Accepted
Submission of supplement to request for an additional site for PUMP-2	3/16/2011	3/18/2011	4/15/2011	Disapproved
Request for 60-day extension to respond to Pump Change Question Set (originally due 5/25/2011)	3/24/2011	3/25/2011	3/30/2011	Accepted
Baclofen Indication	5/13/2011	5/16/2011		

Withdrawal of Baclofen Indication	5/19/2011	5/20/2011	6/15/2011	Withdrawal Accepted
Response to Pump Change Question Set	5/20/2011	2/23/2011	6/17/2011	Approved
Final Report for PUMP-2	7/15/2011	7/18/2011	8/11/2011	Accepted

The Primary Regulatory Review Period (PMA)

Description	**Submission Date**	**FDA Receipt Date**	**FDA Letter Issue Date**	**FDA Response**
Submission of Module 1 of the Premarket Approval Application ("PMA")	8/24/07	8/27/07	11/9/07	deficiency letter
Response to FDA's letter of 11/9/07 re: Module 1	3/18/08			
Submission of Module 2 of PMA	1/31/08	2/5/08	6/6/08	deficiency letter
Submission of Module 3 of PMA	12/13/07	12/18/07	3/21/08	deficiency letter
Response to FDA's questions re: Module 3	4/1/08			
Submission of Module 4 of PMA	4/3/08	4/11/08	7/1/11	deficiency letter
FDA received all Modules and filed PMA submission		4/11/08		
Submission of Panel Review Amendment	6/6/08	6/9/08	7/18/08	deficiency letter
Submission of 100 Day PMA Review Amendment	6/17/08	6/18/08	7/18/08	deficiency letter
Submission of amendment concerning Module 2, correcting company names and relationships	6/26/08	6/30/08	7/18/08	deficiency letter

Exhibit G

Response to Question 4 from 7/18/08 FDA Letter re: drug stability	9/4/08	9/5/08	10/31/08	deficiency letter
First response to Question 1 from 7/18/08 FDA letter		9/9/08	11/4/08	deficiency letter
Second response to Question 1 from 7/18/08 FDA letter	11/25/08	11/26/08	8/19/09	deficiency letter
Extension Request for Prometra® programmable Infusion Pump System	1/14/09	1/15/09	8/19/09	deficiency letter
Response from InSet to FDA Deficiency Letter dated 7/18, 08	3/14/09	3/16/09	8/19/09	deficiency letter
Response from InSet to FDA letter dated 7/31/08	4/9/09	4/10/09	8/19/09	deficiency letter
Call with FDA re: letter dated 7/31/08	4/9/09			
Response to FDA letter dated 5/12/09	6/12/09	6/16/09	8/19/09	deficiency letter
Submission from InSet of a PMA Amendment & Response to FDA letter dated 8/18/09	10/30/09	11/2/09	8/5/10	deficiency letter
Submission of Sterilization Testing (Section 2, part V)		11/23/09	8/5/10	deficiency letter
Unknown Amendment	3/11/10	3/11/10	8/5/10	deficiency letter
Amendment to change applicant's name to Medasys	11/29/10	11/30/10		Entered Amendment
Submission of PMA Amendment & Response to FDA letter dated 8/5/10	1/30/11	1/31/11	7/1/11	deficiency letter
Submission of PMA Amendment & response to FDA letter dated 7/1/11, withdrawing component material and manufacturing changes	7/22/11	7/25/11	2/7/12	Approved
Submission of PMA Amendment to include signed clinical form 3674	11/29/11	11/30/11	2/7/12	Approved

FDA gives approval to PMA with filter seal, suture wings, cannula strain relief, and guidewire manufacture by BARD			2/7/12	
Submission of amendment to Final Labeling	2/23/12	2/27/12	3/14/12	
Submission of amendment to change name of applicant to Flowonix Medical, Inc.	3/2/12	3/5/12		Approved

The Supplemental Regulatory Review Period[*]

Description	Submission Date	FDA Receipt Date	FDA Response Date	FDA Response
Submission of supplement for final PAS protocol (clinical)	3/5/12	3/6/12	5/3/12	Approved
Submission of supplement for final PAS protocol (stability)	3/5/12	3/6/12	5/4/12	Approved
Submission of supplement for final PAS protocol (L-E)	3/5/12	3/6/12	5/4/12	Approved
Submission of supplement for MRI Conditional (real time)	4/19/12	4/20/12		Deficiency
Submission of supplement for a change in the guidewire supplier	4/19/12	4/20/12		Pending
Submission of supplement for a change in the suture wing supplier	4/19/12	4/20/12		Pending
Submission of supplement for a change in the filter seal supplier	4/19/12	4/20/12		Pending

* To date, Flowonix Medical has not received permission from the FDA to use or market the Medical Device until a supplemental review of the Medical Device is completed to determine whether a different supplier of the guidewire, suture wing, and filter seal components of the Medical Device are acceptable. The previous supplier of these parts (BARD) stopped production of these components during the pendency of the Medical Device's regulatory review.

EXHIBIT H

Statement of Patent Term Extension Eligibility and Statement of the Length of Extension Claimed

EXHIBIT H

STATEMENT OF THE APPLICANT'S OPINION THAT THE VALVE PATENT IS ELIGIBLE FOR EXTENSION AND A STATEMENT AS TO THE LENGTH OF THE EXTENSION CLAIMED

Reason for Which an Interim Extension Is Available

In the opinion of Flowonix Medical, Inc., ("Applicant"), U.S. Patent No. 5,368,274 (the "Valve Patent") is eligible for an interim patent term extension pursuant to 35 U.S.C. § 156(d)(5). Applicant is currently only petitioning for a one-year extension under § 156(d)(5) until the earlier of one year from the current expiration date of the patent or regulatory approval from the Food and Drug Administration. Applicant submits that the Valve Patent satisfies all the requirements for an interim extension.

(1) ***35 U.S.C. § 156(a).*** The Valve Patent claims a medical device.

(2) ***35 U.S.C. § 156(a)(1).*** The term of the Valve Patent has not expired before submission of the instant application.

(3) ***35 U.S.C. § 156(a)(2).*** The term of the Valve Patent has never been extended under 35 U.S.C. § 156(e)(1).

(4) ***35 U.S.C. § 156(a)(3).*** The instant application for interim patent term extension is being submitted by an authorized agent of the record owner of the Valve Patent, Flowonix Medical.

(5) ***35 U.S.C. § 156(a)(4).*** The pending product for which approval is sought, Prometra® Programmable Implantable Pump (the "Medical Device"), has been and is continuing to be subject to a regulatory review period before its commercial marketing or use as evident from Exhibit E and Exhibit F.

(6) ***35 U.S.C. § 156(a)(5)(A).*** The first commercial marketing of the Medical Device will follow the approval of request for approval for the commercial marketing or use of the Medical Device.

(7) ***35 U.S.C. § 156(c)(4).*** No other patent has been extended under 35 U.S.C. § 156(e)(1) for the same regulatory review period as the pending Medical Device.

(8) Applicant reasonably believes that it will receive final approval from the Food and Drug Administration ("FDA") for the Medical Device.

The length of interim extension of the term of the Valve Patent claimed by Applicant is one (1) year.

Calculation of Term Extension

Applicant submits that the maximum length of term extension available for the Valve Patent based on approval of the Medical Device, when approved, will be five (5) years, and the length of extension will be determined as follows.

As defined in 37 C.F.R. § 1.777, the length of the regulatory review period for a medical device is the sum of (1) and (2) below:

(1) The number of days in the period beginning on the date a clinical investigation on humans involving the device was begun and ending on the date an application was initially submitted with respect to the device under section 515 of the Federal Food, Drug, and Cosmetic Act; and

(2) The number of days in the period beginning on the date the application was initially submitted with respect to the device under section 515 of the Federal Food, Drug, and Cosmetic Act, and ending on the date such application was approved under such Act.

The period specified by (1) is the number of days in the period beginning on the date IDE # G060192 became effective (FDA gave full approval on 1/3/2007) and ending on the date PMA No. P080012 was submitted (the FDA filed a submission of the four PMA Modules on 4/1/2008 as a complete PMA). This period is 455 days.

The period specified by (2) is ongoing, but the period to date has been at least the number of days in the period beginning on the date PMA NO. P080012 was submitted until the date the present application for interim patent term extension, which is August 30, 2012. This period is 1611 days.

Pursuant to 37 C.F.R. § 1.777(d), Applicant expects that the length of the extension available for the Valve Patent will be the maximum allowed, which is five years. The term of the Valve Patent as extended was calculated as follows:

(1) ***37 C.F.R. § 1.777(d)(1)(i).*** The Valve Patent issued on November 29, 1994. The number of days in periods (1) and (2) above that were on and before the date on which the patent issued is zero (0) days. Therefore, period (1) still totals 455 days and period (2) still totals 1611 days.

(2) ***37 C.F.R. § 1.777(d)(1)(ii).*** Applicant submits that it has acted with due diligence during the entire regulatory review period. Accordingly, the period specified by 37 C.F.R. § 1.777(d)(1)(ii) is zero (0) days. Therefore, period (1) still totals 455 days and period (2) still totals 1611 days.

(3) ***37 C.F.R. § 1.777(d)(1)(iii).*** The period specified by 37 C.F.R. § 1.777(d)(1)(i) is 455 days. One half of this period is 227.5 days (treated as 227 days). Therefore, period (1) totals 227 days and period (2) still totals 1611 days. Summing periods (1) and (2) together results in a period of 1888 days.

(4) ***37 C.F.R. § 1.777(d)(2).*** The original term of the Valve Patent, as there are no terminal disclaimers, expires September 17, 2012. Adding 1888 days to this current patent term would extend the term of the Valve Patent to November 18, 2017.

(5) ***37 C.F.R. § 1.777(d)(3).*** PMA No. P080012 has not been fully approved yet. If the PMA were approved on August 30, 2012, the date specified by 37 C.F.R. § 1.777(d)(3) would be August 30, 2026. Accordingly, the date specified by 37 C.F.R. § 1.777(d)(3) can be no earlier than August 30, 2026.

(6) ***37 C.F.R. § 1.777(d)(4).*** The earlier of November 18, 2017 and August 30, 2026 is November 18, 2017.

(7) ***37 C.F.R. § 1.777(d)(5).*** The term of the Valve patent expires on September 17, 2012. Adding five years results in a date of September 17, 2017. The earlier of this date and the date specified by 37 C.F.R. § 1.777(d)(4) is September 17, 2017.

Thus, pursuant to 37 C.F.R. § 1.777(d), Applicant expects that the length of the extension available for the Valve Patent will be the maximum allowed, which is five years. Applicant also expects that the applicable regulatory review period under 35 U.S.C. § 156(g) that began for the Medical Device will extend beyond September 17, 2012, the date when the Valve Patent expires.

Applicant therefore requests an interim one-year extension of the term of U.S. Patent No. 5,368,274.

EXHIBIT I

Letter from the FDA Dated February 7, 2012

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Room –WO66-G609
Silver Spring, MD 20993-0002

FEB - 7 2012

Ms. Jill Schweiger
Vice President, Clinical Studies and Regulatory Affairs
Medasys, Incorporated
500 International Drive
Suite 200
Mount Olive, New Jersey 07828

Re: P080012
Prometra Programmable Infusion Pump System
Filed: April 11, 2008
Amended: June 9, 2008; June 18, 2008; June 30, 2008; September 5, 2008; September 8, 2008; November 26, 2008; January 15, 2009; March 16, 2009; April 10, 2009; June 16, 2009; November 2, 2009; November 23, 2009; March 11, 2010; December 8, 2010; January 31, 2011; July 25, 2011; and November 30, 2011
Procode: LKK

Dear Ms. Schweiger:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your premarket approval application (PMA) for the Prometra Programmable Infusion Pump System.

The Prometra Programmable Infusion Pump System is indicated for intrathecal infusion of Infumorph (preservative-free morphine sulfate sterile solution) or preservative-free sterile 0.9% saline solution (Sodium Chloride Injection, USP).

We are pleased to inform you that the PMA is approved. You may begin commercial distribution of the device in accordance with the conditions of approval described below.

The sale and distribution of this device are restricted to prescription use in accordance with 21 CFR 801.109 and under section 515(d)(1)(B)(ii) of the Federal Food, Drug, and Cosmetic Act (the act). FDA has determined that this restriction on sale and distribution is necessary to provide reasonable assurance of the safety and effectiveness of the device. Your device is therefore a restricted device subject to the requirements in sections 502(q) and (r) of the act, in addition to the many other FDA requirements governing the manufacture, distribution, and marketing of devices.

Expiration dating for the Prometra Programmable Infusion System has been established and approved for each separately packaged component as follows:

- Prometra Pump: 2 years
- Intrathecal Catheter Kit: 2.75 years
- Catheter Access Port Kit: 4.91 years
- Pump Refill Kit: 4.91 years
- Tunneler Kit: 4.91 years

Continued approval of this PMA is contingent upon the submission of periodic reports, required under 21 CFR 814.84, at intervals of one year (unless otherwise specified) from the date of approval of the original PMA. Two copies of this report, identified as "Annual Report" (please use this title even if the specified interval is more frequent than one year) and bearing the applicable PMA reference number, should be submitted to the address below. The Annual Report should indicate the beginning and ending date of the period covered by the report and should include the information required by 21 CFR 814.84.

In addition to the above, and in order to provide continued reasonable assurance of the safety and effectiveness of the device, the Annual Report must include, separately for each model number (if applicable), the number of devices sold and distributed during the reporting period, including those distributed to distributors. The distribution data will serve as a denominator and provide necessary context for FDA to ascertain the frequency and prevalence of adverse events, as FDA evaluates the continued safety and effectiveness of the device.

In addition to the Annual Report requirements, you must provide the following data in post-approval study reports (PAS). Two copies, identified as "PMA Post-Approval Study Report" and bearing the applicable PMA reference number, should be submitted to the address below.

1. As a condition of approval, you have agreed to conduct the post-approval studies (A prospective, non-randomized, open-label, multicenter study to evaluate the long-term safety of the Prometra Programmable Pump System). The PAS protocol includes, but is not limited to the following items:

   a. It will be performed at up to 30 centers in the US.

   b. A total of 400 subjects will be enrolled to ensure at least 300 will be followed for five years.

   c. The primary endpoint is to assess the 5-year rate of granuloma formation. The primary hypothesis is that the 5-year granuloma rate is less than 3% (with a 3% margin). Secondary endpoints are to assess the long-term device performance including: (1) Pump failure (time to occurrence, type, and number of occurrences), (2) pump battery life, (3) device-related-adverse events, and (4) device-related serious adverse events. The study will also include a descriptive evaluation of the effect of race and ethnicity on granuloma formation, and the effect of alternative

drugs on granuloma formation.

d. The study participants will consist of two groups: (1) Group A: newly enrolled study subjects, and (2) Group B: subjects previously enrolled in the PUMP I or PUMP II study. Approximately 25% patients enrolled in PUMP I and PUMP II studies will be enrolled into Group B. Subjects shall be seen at least once every 90 days (± 30 days) from the date of implantation (Group A) or PAS enrollment (Group B) throughout the study.

2. As a condition of approval, you have agreed to conduct the following non-clinical post-approval studies: Post-Approval Extended Use Stability (Rev C) and Post-Approval Leachables (Rev C). This PAS is a non-clinical study to evaluate the long-term interactions between your device system and the indicated drug product. The protocols include, but are not limited to, the following items:

a. The primary objectives of the studies are to demonstrate:

Extended Use Stability Study

i. Stability of Infumorph in Prometra infusion pumps for a period of 90 days;

ii. Stability of Infumorph after multiple refills over the lifetime of the pump (10 years) in the pump reservoir; and

iii. Pump function by assessing pump flow rate throughout study duration.

Leachables Study

iv. To perform controlled extraction studies to assess acceptable limits of any identified leachable materials (in consideration of the ICH Q3B and PQRI publication "Safety Thresholds and Best Practices for Extractables and Leachables in Orally Inhaled and Nasal Drug Products.")

v. In parallel with the activities performed in accordance with the controlled extraction study, samples will be placed within the appropriate chambers and pulled at the appropriate time points. Samples at each pull point will be stored and placed for routine testing once the methods are established from the controlled extractable study.

b. Study Samples: Sixteen (16) Prometra pumps will be included in the Extended Use Stability study. Eight (8) Prometra pumps will be included in the Leachables study.

c. Endpoints:

Extended Use Stability Study

i. Assay will be compared to a control solution at each time point.

ii. Related substances, unknown impurities, appearance and pH will be reported. Related substances and unknown impurities will be assessed for safety impact at each time point.

iii. As the study progresses, appropriate criteria for identified degradation products will be established in accordance with ICH Q3B and PQRI recommendations and will be supported with appropriate safety justifications. The established specifications will be submitted to FDA for evaluation.

iv. Flow rate accuracy shall be within ±15% of the set point at each timepoint.

Leachables Study

v. Results from leachable analysis over the sample periods will be assessed for safety impact at each time point.

vi. As the study progresses, appropriate criteria for the identified leachables will be established in accordance with ICH Q3B and PQRI recommendations and supported with appropriate safety justifications. The established specifications will be submitted to FDA for evaluation.

d. The overall study duration will be 126 months after FDA's PMA Approval, which includes the analysis and submission of the Final Study Report.

Please be advised that the results from this study should be included in the labeling as these data become available. Any updated labeling must be submitted to FDA in the form of a PMA Supplement.

FDA would like to remind you that you are required to submit PAS Progress Reports every six months during the first two years and annually thereafter. The reports should clearly be identified as Post-Approval Study Report. The progress reports will include results and analysis of testing conducted on samples at time points preceding the progress report. Deviations should also be identified in the progress reports. Two copies, identified as "PMA Post-Approval Study Report" and bearing the applicable PMA reference number, should be submitted to the address below. For more information on post-approval studies, see the FDA guidance document entitled, "Procedures for Handling Post-Approval Studies Imposed by PMA Order" http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance /GuidanceDocuments/ucm070974.htm

Be advised that the failure to conduct any such study in compliance with the good clinical laboratory practices in 21 CFR part 58 (if a non-clinical study subject to part 58) or the institutional review board regulations in 21 CFR part 56 and the informed consent regulations in 21 CFR part 50 (if a clinical study involving human subjects) may be grounds for FDA withdrawal of approval of the PMA.

Within 30 days of your receipt of this letter, you must submit a PMA supplement that includes complete protocols of your post-approval studies. Your PMA supplement should be clearly labeled as a "Post-Approval Study Protocol" and submitted in triplicate to the address below. Please reference the PMA number above to facilitate processing. If there are multiple protocols being finalized after PMA approval, please submit each protocol as a separate PMA supplement. For more information on post-approval studies, see the FDA guidance document entitled, "Procedures for Handling Post-Approval Studies Imposed by PMA Order" at the web site stated above.

Before making any change affecting the safety or effectiveness of the device, you must submit a PMA supplement or an alternate submission (30-day notice) in accordance with 21 CFR 814.39. All PMA supplements and alternate submissions (30-day notice) must comply with the applicable requirements in 21 CFR 814.39. For more information, please refer to the FDA guidance document entitled, "Modifications to Devices Subject to Premarket Approval (PMA) - The PMA Supplement Decision-Making Process" (www.fda.gov/MedicalDevices /DeviceRegulationandGuidance/GuidanceDocuments/ucm089274.htm).

You are reminded that many FDA requirements govern the manufacture, distribution, and marketing of devices. For example, in accordance with the Medical Device Reporting (MDR) regulation, 21 CFR 803.50 and 21 CFR 803.52, you are required to report adverse events for this device. Manufacturers of medical devices, including in vitro diagnostic devices, are required to report to FDA no later than 30 calendar days after the day they receive or otherwise becomes aware of information, from any source, that reasonably suggests that one of their marketed devices:

1. May have caused or contributed to a death or serious injury; or

2. Has malfunctioned and such device or similar device marketed by the manufacturer would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.

Additional information on MDR, including how, when, and where to report, is available at www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm.

In accordance with the recall requirements specified in 21 CFR 806.10, you are required to submit a written report to FDA of any correction or removal of this device initiated by you to: (1) reduce a risk to health posed by the device; or (2) remedy a violation of the act caused by the device which may present a risk to health, with certain exceptions specified in 21 CFR

806.10(a)(2). Additional information on recalls is available at www.fda.gov/Safety/Recalls/IndustryGuidance/default.htm.

CDRH does not evaluate information related to contract liability warranties. We remind you; however, that device labeling must be truthful and not misleading. CDRH will notify the public of its decision to approve your PMA by making available, among other information, a summary of the safety and effectiveness data upon which the approval is based. The information can be found on the FDA CDRH Internet HomePage located at www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/PMAApprovals/default.htm. Written requests for this information can also be made to the Food and Drug Administration, Dockets Management Branch, (HFA-305), 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. The written request should include the PMA number or docket number. Within 30 days from the date that this information is placed on the Internet, any interested person may seek review of this decision by submitting a petition for review under section 515(g) of the act and requesting either a hearing or review by an independent advisory committee. FDA may, for good cause, extend this 30-day filing period.

Failure to comply with any post-approval requirement constitutes a ground for withdrawal of approval of a PMA. The introduction or delivery for introduction into interstate commerce of a device that is not in compliance with its conditions of approval is a violation of law.

You are reminded that, as soon as possible and before commercial distribution of your device, you must submit an amendment to this PMA submission with copies of all approved labeling in final printed form. Final printed labeling that is identical to the labeling approved in draft form will not routinely be reviewed by FDA staff when accompanied by a cover letter stating that the final printed labeling is identical to the labeling approved in draft form. If the final printed labeling is not identical, any changes from the final draft labeling should be highlighted and explained in the amendment.

All required documents should be submitted in triplicate, unless otherwise specified, to the address below and should reference the above PMA number to facilitate processing. One of those three copies may be an electronic copy (eCopy), in an electronic format that FDA can process, review and archive (general information: http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/ucm134508.htm; clinical and statistical data: http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/ucm136377.htm)

U.S. Food and Drug Administration
Center for Devices and Radiological Health
PMA Document Mail Center – WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

If you have any questions concerning this approval order, please contact LCDR Alan M. Stevens at 301-796-6294.

Sincerely yours,

Anthony D. Watson

Anthony D. Watson, B.S., M.S., M.B.A.
Director
Division of Anesthesiology, General Hospital,
Infection Control and Dental Devices
Office of Device Evaluation
Center for Devices and Radiological Health